Draft Responses to Comments on the Final Public Review Draft: "Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act"

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Response to Comments on Final Public Review Draft Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act

July, 2001

Responses to Comments on Formaldehyde from the Composite Panel Association

Comment by B. Landry of Venable, Attorneys at Law, for the Composite Panel Association ("CPA"), formerly the National Particleboard Association

Comment 1: CPA strongly supports the decision of OEHHA, which was endorsed by the Scientific Review Panel, to remove formaldehyde from Tier 1 status. … The reasons that formaldehyde was removed from Tier 1 were fully explained by the OEHHA staff and endorsed by consensus at the SRP's June 15, 2001 meeting. The studies simply do not support such a listing.

Response 1: OEHHA thanks the commenter for the support. Although the consensus was that the studies were not sufficient to place formaldehyde in Tier 1, OEHHA did find that there was evidence of possible differential effects of formaldehyde on children. The decision to remove formaldehyde from Tier 1 was based on the conclusion by OEHHA that other TACs deserved higher priority. Although the prioritization process to be used in subsequent stages of the implementation of the Children's Environmental Health Protection Act (SB25) has yet to be determined, the evidence identified in this report will be taken into account when formaldehyde is eventually considered in detail (as is required for all identified TACs).

Comment 2: Another strongly encouraging development, not discussed at the meeting, is the publication of a new risk assessment of formaldehyde by the CIIT Research Centers, Formaldehyde: Hazard Characterization and Dose-Response Assessment for Carcinogenicity by the Route of Inhalation. This state of the art, peer-reviewed work was developed over many years with the cooperation and guidance of personnel from the EPA and Health Canada. It showed a dramatically lower risk than had previously been assumed. … It adds weight to the decision of OEHHA to remove formaldehyde from Tier 1.

Response 2: OEHHA takes note of the material presented in this comment. The information presented bears primarily on cancer risk in adults. OEHHA has expressed a general concern that carcinogens may have differential impact on infants and children, and this was taken into account in considering the priority given to formaldehyde. However, neither the commenter nor OEHHA have identified evidence of a differential carcinogenic effect specifically of formaldehyde on children. OEHHA is familiar with the dose-response analyses described by the commenter, but emphasizes that the results of these calculations have no direct bearing on the current process of prioritization under SB25. Indeed, it might be concluded that the emphasis on the clonal expansion model in the formaldehyde analysis provides a clear mechanistic and mathematical basis for expecting that there would be a greater sensitivity to the carcinogenic effect at younger ages. However, as OEHHA pointed out in the introduction to the document, such general considerations were given a lower weight in the prioritization than experimental data with the specific compound being evaluated.

Comments of the American Chemistry Council Carbon Disulfide Panel

The Carbon Disulfide Panel of the American Chemistry Council submitted comments in response to the notice regarding the prioritization of the Toxic Air Contaminants (TACs) for the California Children's Environmental Health Protection Act (SB25) in a letter dated July 13, 2001.

Comment 1: The Panel supports OEHHA's reliance on the benchmark concentration (BMC) methodology used by the United States Environmental Protection Agency (EPA) and Environment/ Health Canada (E/H Canada) in determining the chronic REL. OEHHA should use methods and assumptions equivalent to those used by EPA in calculating the BMC (in the course of calculating the reference concentration (RfC) for carbon disulfide).

Response 1: An early draft of a carbon disulfide chronic REL summary was presented for comment as part of the Hot Spots program's Technical Support Documents. This evaluation has not yet been completed, but OEHHA will invite public comment on a revised draft carbon disulfide REL some time in the future. OEHHA appreciates the Carbon Disulfide Panel's comments about the determination of a chronic reference exposure (REL) for carbon disulfide, which will be reviewed during the preparation of that revised draft. However, we wish to emphasize that this is a separate process from OEHHA's work for the Children's Environmental Health Protection Act. It does not appear to OEHHA that any of the material submitted has a bearing on the issue of possible differential susceptibility of infants and children to the toxicity of carbon disulfide, which was the issue presented in the prioritization document currently under consideration by the Scientific Review Panel.

Comment 2: OEHHA should not use certain of the procedures and assumptions E/H Canada used in calculating the BMC for purposes of determining the Tolerable Concentration (TC). E/H Canada's methodology for calculating the BMC would be appropriate, only if the appropriate assumptions regarding the percentile limit that defines "abnormal" in the control population and the percentage assumed for determining the benchmark response for peroneal motor nerve conduction velocity are made.

Response 2: See response to Comment 1.

Comment 3: OEHHA should apply no more than an overall 15-fold uncertainty factor in establishing the chronic REL from the BMC, which is smaller than that used by EPA and considerably smaller than that used by E/H Canada in their calculations of the reference dose (RfD) and the TC, respectively, for carbon disulfide.

Response 3: See response to Comment 1.

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July, 2001

Response to Comments on Phthalate Esters by the American Chemistry Council

The American Chemistry Council Phthalate Esters Panel (panel) submitted comments on OEHHA's proposed prioritization of Toxic Air Contaminants (TACs) under the Children's Environmental Health Protection Act in a letter from Courtney Price dated July 12,2001.

Comment: In OEHHA's Final Public Review Draft, Appendix A erroneously includes butyl benzyl phthalate (BBP) and bis(2-ethylhexyl)adipate (DEHA) in lists of TACs. The Panel strongly urges OEHHA to revise the tables in Appendix A to distinguish chemicals that have not been identified as TACs - such as BBP and DEHA - from those that are TACs. Appendix A contains two tables: Table A -"List of Toxic Air Contaminants", and Table B -"List of Toxic Air Contaminants that dropped out of the process after the initial ranking". The table names indicate that all substances listed within are TACs. However, BBP and DEHA are not classified as TACs by the California Air Resources Board (CARB). In 1999, CARB released an update to the Toxic Air Contaminants list. In that release, CARB classified both BBP and DEHA as Category IVb substances ("Substances NOT identified as Toxic Air Contaminants, known to be emitted in California, and are TO BE EVALUATED for entry into Category III")

Substances in Category IVb which are evaluated may enter Category III, and, in the case of BBP and DEHA, would be designated as Category IIIb ("NOT identified as Toxic Air Contaminants"). Those in Category III are nominated for development of health values or additional health values. Even after development of such health values, there still remains a long process before a substance is identified as a TAC by CARB. Thus, BBP and DEHA are several steps away from even being considered for identification as TACs.

Moreover, the Panel does not believe BBP and DEHA will ever be classified as TACs because of their low toxicity and low emissions in California. In February 1999, Solutia Inc. submitted comments that demonstrate that BBP and DEHA air emissions in California are not likely to pose toxicity concerns, and the Panel has supported those comments. As was shown in the Solutia Inc. comments, BBP and DEHA exhibit toxicity only at very high doses, and air emissions of BBP and DEHA from stationary sources in California are low, such that fence line concentrations are expected to be well below health benchmarks. Furthermore, EPA has removed both BBP and DEHA from the list of toxic chemicals under the Emergency Planning and Community Right-to-Know Act (EPCRA). That is, EPA has determined that environmental releases of these chemicals are not known to cause, nor reasonably anticipated to cause, serious, acute or chronic effects in humans nor significant adverse effects on the environment.

The Panel believes that an OEHHA document, which lists BBP and DEHA as TACs, would cause great confusion and might lead to unwarranted control actions and misallocation of scarce resources. It is to be expected that documentation originating from OEHHA will be heavily relied upon by the general public. Therefore, it is imperative that the information in that document is complete and accurate. Because BBP and DEHA are not designated as TACs, OEHHA should revise the tables in Appendix A so it is clear that chemicals such as BBP and DEHA are not TACs. This is particularly important since we believe BBP and DEHA probably

never will be designated as TACs, given their toxicological and exposure profiles.

Response: OEHHA thanks the commenter for pointing out that BBP and DEHA, which are on the list for future evaluation as TACs (Category IVb) were erroneously included in the tables along with substances identified as TACs (Category I). OEHHA will amend the tables in the final version of the report accordingly. This action by OEHHA implies no judgment at this time on the toxicity data for these compounds: these may eventually be evaluated by ARB and OEHHA as part of the TAC prioritization process.

Response to Comments on Toluene and Xylene by the American Chemistry Council

The Toluene & Xylene VCCEP Consortium (the "Consortium") of the American Chemistry Council submitted comments in response to the notice regarding the prioritization of the Toxic Air Contaminants (TACs) for the California Children's Environmental Health Protection Act (SB25) in a letter from Courtney M. Price dated July 12, 2001.

[The Consortium has sponsored toluene and xylene under the U.S. Environmental Protection Agency (EPA) Voluntary Children's Chemical Evaluation Program (VCCEP).]

Comment: It's the Consortium's understanding that the Scientific Review Panel (SRP) has recommended that toluene and xylene be added to the list of priority TACs. The Consortium is writing to encourage OEHHA not to make toluene or xylene a Tier 1 or Tier 2 priority and not to undertake any additional reviews of these chemicals until they have been reviewed under VCCEP. The Consortium believes this will avoid an unnecessary duplication of effort and that OEHHA could utilize the review of these chemicals under the VCCEP, which includes an independent scientific peer consultation as part of the review.

Response: The SRP did not recommend including toluene and xylene in the list of five high priority TACs for listing under SB25, nor were they included in either Tier 1 or Tier 2 of the list of candidate compounds proposed by OEHHA. However, because they are listed as Toxic Air Contaminants in California, they will be examined some time in the future under the mandate of SB25. Relevant data from the Voluntary Children's Chemical Evaluation Program or any other peer-reviewed scientific sources should be submitted for consideration at that time.

July, 2001

Responses to Comments on Vinyl Chloride by the American Chemistry Council

Comment 1: On April 6, 2001, the Health Committee submitted a detailed comment on the Chemical Toxicity Summary for vinyl chloride provided with the March 2001 version of the draft Prioritization document. OEHHA' s response to this comment recognized that there were serious deficiencies in the background document for vinyl chloride. We note that the revised Chemical Toxicity Summary has been improved by eliminating the discussion of unit risk estimates (potency factors). In other contexts, we urge OEHHA to continue to address the disparities between its unit risk estimate for vinyl chloride and the more recent estimates provided by the U.S. Environmental Protection Agency in the Toxicological Review now posted on its Integrated Risk Information System (IRIS). These inconsistencies are due both to the use of an inappropriate cancer bioassay (Drew et al.) for derivation of the cancer slope factor, and to OEHHA' s reliance on default factors that less accurately predict target tissue exposure than newer methodologies, such as the physiologically-based pharmacokinetic (PB-PK) modeling that EPA relied upon. In the April 6 submission, the Health Committee also pointed out that the earlier background document failed to address the major epidemiology studies of vinyl chloride workers that have been updated over the past ten years. OEHHA recognized that it inadvertently had omitted discussion of these studies and indicated that the draft document would be revised to include the later studies and that "[t]he later studies will be evaluated together with the older ones to arrive at a more balanced summary of all the results. The revised Chemical Toxicity Summary, however, continues to state, relying on the older studies, that "[f]ive of eight studies that examined the association of brain cancer with vinyl chloride exposure found a statistically-significant positive association between brain cancer and vinyl chloride exposure. As indicated in our comment, when the updates of these studies are considered, as was done by EPA in its recent Toxicological Review, it becomes clear that the epidemiological evidence is not sufficient justifiably to conclude that there is an association between vinyl chloride exposure and brain cancer. This has been the judgment of several independent reviewers, including Sir Richard Doll and Aaron Blair of the National Cancer Institute, as noted in our earlier comment. We urge OEHHA to move forward with the promised evaluation "to arrive at a more balanced summary of all the results" when it revises the current draft Chemical Toxicity Summary for vinyl chloride.

Finally, OEHHA recognized the importance of including the reproductive and developmental toxicity study sponsored by the Health Committee in its review, and this remains to be done.

Response 1: The purpose of the Chemical Toxicity Summary for Vinyl Chloride was to set forth the evidence that vinyl chloride may pose a differential risk to children. The main evidence for this is the animal data, which show that exposure to animals early in life results in a greater carcinogenic effect than exposure spread out over the lifetime of the animals. Human epidemiological data was briefly summarized to show that it is also

well established that vinyl chloride is a known human carcinogen. The evidence relating specifically to brain cancer has been reviewed and discussed in previous OEHHA documents, including the Public Health Goal for Drinking Water document dated September 2000 available on the OEHHA website. The epidemiological data for occupational exposures to vinyl chloride are summarized in Table 14 of that document and discussed in the accompanying text. New epidemiological studies and new evaluations of those studies may continue to appear in the future. OEHHA will need to consider all available data and interpretations before considering any actions with regard to vinyl chloride. We realize that in the response to the first public comment period we indicated we would expand our table describing the epidemiology studies and add in newer studies. In the final analysis, the epidemiological data do not provide any useful information to address the question of differential sensitivity between young and mature humans, and thus we eliminated the table. The reader is now referred to the Public Health Goal document for more information on the epidemiology studies.

OEHHA has reviewed the reproductive and developmental toxicity study referred to in the comment, and will consider it together with other related studies in its future consideration of vinyl chloride. These studies were conducted by Huntingdon Life Sciences for the Chemical Manufacturers Association. In both studies rats were exposed to vinyl chloride in air at 0, 10, 100 and 1100 ppm. No adverse reproductive effects were observed. Therefore the reproductive study authors conclude that the NOEL for reproductive effects is greater than 1100 ppm. In the developmental study an increase in kidney weight was observed in the dams exposed to 10 ppm vinyl chloride. No developmental effects were observed in the offspring at any exposure level. The study concluded that the NOEL for maternal toxicity was 10 ppm, and for developmental toxicity the NOEL was 1100 ppm. As these are negative results they are not likely to play a major part in the evaluation of differential toxicity of vinyl chloride to infants and children, but they should be considered together with other studies in future evaluations of vinyl chloride toxicity.

Comment 2: The revised Chemical Toxicity Summary for vinyl chloride provides a more complete discussion of the data supporting OEHHA' s position that infants and children may be more sensitive to the carcinogenic effects of vinyl chloride than are adults. The Health Committee continues to believe that any differential carcinogenic effect on children from vinyl chloride is highly uncertain. As noted in our earlier comment, many chemicals require microsomal P-450 enzyme formation for metabolic activation. If these enzymes are not fully developed in infants and children, they will be less susceptible to toxic effects of chemicals that require such activation, not more so. Moreover, as discussed in more detail in our earlier comment, strict federal and state regulation has reduced greatly the possibility that children will ever be exposed to vinyl chloride. As OEHHA recognizes, vinyl chloride has not been detected in the ambient air in California at or above the detection limit, except for measurements taken adjacent to vinyl chloride-related industries and landfills.

Response: OEHHA agrees that **if** the microsomal P-450 enzymes that are required for metabolic activation of vinyl chloride were not fully developed in infants and children, and if detoxification pathways remained unchanged, one might expect infants and children to be less sensitive to vinyl chloride than adults. However, the animal experiments cited in the Chemical Toxicity Summary demonstrate that young animals are more sensitive than adults to the carcinogenic effects of vinyl chloride. The final carcinogenic effect depends on both toxicokinetic factors (e.g. activation and deactivation of toxic metabolites), and toxicodynamic factors. We do not know at present which of these factors are responsible for the increased sensitivity of young animals.

OEHHA has repeatedly acknowledged that vinyl chloride is not a general ambient air exposure problem.

Response to Comments from the Natural Resources Defense Council (Diane A. Bailey, M.S., Staff Scientist; Gina Solomon, M.D., M.P.H., Senior Scientist).

Comment 1: We strongly support the listing of Diesel Exhaust Particulate and PAHs as Tier 1 TACs.

We applaud OEHHA for listing Diesel Exhaust Particulates (DEP) as a Tier I TAC. Given findings of high cancer risks, childhood asthma and a multitude of other health problems associated with DEP, we believe this pollutant should be of the utmost priority for consideration of new standards to protect children's health. The relatively new data linking diesel exhaust particulate to immunological changes in the airways that create the inflammatory effects seen in asthma are particularly important in the context of risks to children. Several epidemiologic studies of children living along major trucking routes have also shown decreased lung function or asthmatic reactions. These data indicate that children may be at particular risk from diesel exhaust particulate.

We also recognize that while PAHs are a component of DEP, they are emitted from other sources as well. It remains somewhat unclear to us why DEP and PAHs cannot be combined, because the toxicity and sources are highly overlapping. However, we do agree that the literature on PAHs does indicate a significant risk to children and we believe that PAHs must be reassessed and better controlled to protect children.

Response 1: OEHHA thanks the NRDC for their supportive comments in relation to the listing of DEP as one of the five initial TACs to be considered under the Children's Environmental Health Protection Act (SB25).

OEHHA also notes the commenters' agreement that PAHs present a significant risk to children. However, OEHHA considers it would be inappropriate to combine the listing of PAHs and DEP under SB25, for three primary reasons:

1. Although many of the health effects of DEP are similar to those of PAHs, there may be some different effects, resulting from other components of DEP, or from the interaction of multiple components.

2. DEP is an important source of environmental exposure to PAHs. However, as documented in the summary, there are a number of other such sources, including industrial emissions, environmental tobacco smoke and some methods of domestic heating or cooking.

3. In the interests of clarity, and compliance with the mandate, OEHHA has generally attempted to maintain correspondence between the categories used in the TAC listing process and those used for the SB25 prioritization. DEP is identified as a TAC separately from the listing of Polycyclic Organic Matter (the inclusive category of which PAHs

form an important and more clearly characterized subset).

Comment 2. Benzene Should Remain a Tier 1 TAC.

NRDC is disappointed that industry comments led to the removal of benzene from Tier 1. We reiterate that the science supporting high exposures and health risks to children is strong. At the June 15th Air Resources Board Scientific Review Panel meeting, OEHHA conceded that they agree with many of the comments that the epidemiological evidence is weak for elevated incidences of childhood leukemia associated with parental exposure to benzene. However, Table 4 of the *Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act,* prepared by OEHHA, 1ists "… studies indicating increased risk of childhood leukemia in children of benzene-exposed workers." as a major reason why benzene was chosen as a Tier 2 TAC. NRDC agrees with the original OEHHA assessment that benzene is associated with leukemia in the children of exposed parents. Because this finding is true for fathers as well as mothers, it's not clear whether the risk is prenatal or is postnatal due to vapors carried home on the father's breath or clothing. The evidence is sufficient to indicate a likely risk to children. Given the fact that benzene is a high volume chemical with toxic hotspots in California, we believe benzene should be moved back into Tier 1.

Response 2: OEHHA assures the commenters that, while due notice was taken of all public comments received, the primary stimulus to the removal of benzene from Tier 1 was that the evidence available for differential impacts of benzene on infants and children is less convincing than that presented for several other agents. Since the statute allows a maximum of five TACs in the initial listing, we were constrained from listing more than five, and chose to defer benzene for the moment due to the relatively weak and largely indirect evidence for differential impacts. In spite of this change in the overall prioritization, OEHHA continues to be concerned about benzene. There are substantial hotspot releases of benzene as well as a relatively high ambient air level. We will continue to monitor the literature for papers that will help define the issue of differential susceptibility to benzene.

Comment 3. Include 1,3-butadiene in the Next Evaluation.

NRDC urges OEHHA to re-evaluate 1,3-butadiene during the next listing process. Based on the relatively high exposures and risks discussed in our earlier comments, 1,3-butadiene should be placed in the Tier 2 group at least. Although the evidence of infant and child toxicity may be somewhat limited, it is nonetheless important, especially given the highly ubiquitous nature of this compound.

Response 3: Although the procedures for any subsequent prioritization under SB25 have yet to be determined, OEHHA shares the commenters' concerns about 1,3-butadiene, and will take these considerations into account at the appropriate time.

Response to Comments on Final Public Review Draft Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act

July, 2001

Response to Comments on Acrolein from Earl Meierhenry, DVM, PhD

Comment 1. Why was there no mention of increased potential acrolein air and drinking water exposure to farm kids following pesticide use? This would increase risk.

The California Pesticide Use Report indicates that several hundred thousand pounds of acrolein pesticide are used each year in California. This is too big to ignore.

Response 1: The acrolein summary noted (under Principal Sources of Exposure) some of acrolein's pesticidal uses. OEHHA will extend this information in the final document by noting that, according to DPR's Annual Pesticide Use Reports for 1996-1999, over 300,000 pounds of acrolein are applied in California each year. (The majority of this is used on rights of way, rather than on farms). It is important to note that the health impacts of pesticides in their pesticidal uses are excluded from consideration under SB25, as explained in the introductory section of the document.

Comment 2. Why was there no mention of the toxic effects reported in the acrolein animal toxicity database used by the Department of Pesticide Regulation?

By Law, that material has been reviewed by state toxicologists at public expense. It should be used. Final reports, not just published information, are available.

Response 2: OEHHA relies upon reports published in the peer-reviewed scientific literature wherever possible, but also considers reports submitted to DPR for regulatory purposes where these contain relevant information which is not available from published sources. There are several studies on acrolein toxicity following oral dosing included in the DPR toxicity database: these were considered to be of limited relevance in assessing impacts of airborne exposures to children. There are two chronic toxicity studies, one in rats and one in dogs. The rat study showed no indication of an adverse effect from acrolein exposure. In the dog study, a decrease in the activated partial thromboplastic time (hypercoagulation) was identified as a possible adverse effect from acrolein exposure (NOAEL = 0.1 mg/kg); however, there is no indication that children might be more sensitive to this endpoint than adults. There are two teratology studies in the database, one in rats and one in rabbits. Neither showed any adverse developmental effects. There are two reproductive studies in the database. In one two-generation study in Crl:CD*(SD)BR rats, a "possible adverse effect" was noted. In this gavage study, there was a high incidence of mortality and respiratory complications that were determined to be due to the dosing protocol. The summary in the database noted that the parental NOAEL in this study was 1 mg/kg (hyperplasia/hyperkeratosis). The only progeny effect was a significant reduction in pup body weights, starting on lactation day 7 for the high dose group (6 mg/kg-day). For males only, this reduction persisted until the end of the study. The progeny NOAEL was determined to be 3 mg/kg (reduced pup weight during lactation), which is a dose level associated with toxicity in the adults. And finally, there are two oral oncogencity studies in the database. There is a mouse study, which showed no evidence of a

treatment-related effect, and there is a rat study that showed pancreatic acinar cell tumors (adenoma and carcinoma) resulting from acrolein exposure.

In addition to the data reviewed and summarized in the toxicity database, we also looked at other information submitted to DPR on acrolein but did not find anything else that would be relevant for the purposes of this document. The OEHHA document is intended to review only data indicating potential to impact children more than adults. Since the data from the DPR toxicity database do not provide information relevant to evaluating any differential impact between children and adults, those data were not incorporated into the document.

July, 2001

Responses to Comments Submitted by Western States Petroleum Association on Diesel Exhaust Particulate

Overall Comment: The Western States Petroleum Association (WSPA), wish to submit these comments on the listing of diesel exhaust particulate (DEP) in the "Tier 1" category and on the background document that OEHHA has prepared on this substance. As you know, WSPA has been actively following this issue for some time and this issue continues to be a high priority for our members.

We note that OEHHA's previous draft placed DEP in the "Tier 2" group because the data for adverse effects on children were primarily indirect and not as strong as for other compounds under consideration. Our reading of the available material indicates that this is still the case with respect to causality, exposure and susceptibility. Therefore, we see no basis to place the material in Tier 1. The rationale presented by OEHHA is based on five lines of evidence; 1) Enhancement of allergic responses; 2) Traffic density studies; 3) General ambient PM10 health effects; 4) PAHs found in DEP; and 5) Developmental and reproductive effects. We provide some very brief comments these issues below.

Comment 1: Enhancement of Allergic Responses

The findings of biochemical changes in response to exposure to DEP are of interest and the potential for an adjuvant response should be investigated more thoroughly (Mauderly, 2001). However it must be emphasized that biochemical indicators are not the same as an observed increase in symptoms, and intratracheal (or intranasal) instillation of high levels of DEP is not the same as inhalation exposure of low levels of DEP. Thus while the findings to date may lead one to hypothesize about effects on asthma and allergy severity, there remains a lack of direct evidence in this area. It remains to be determined whether the adjuvant effect is significant at current environmental exposure levels, and whether the effect is unique to DEP. The level of evidence at this point in time does not justify the placement of DEP in Tier1. This is especially true when one compares the strength of evidence for diesel with other toxic air contaminants (e.g. formaldehyde) that have been reviewed in this process and that were not included in the Tier 1 list.

Response 1: Diesel exhaust particulate matter causes adverse immune system effects that may result in adverse health outcomes (e.g. possible exacerbation of asthma and allergic rhinitis) (Diaz-Sanchez *et al*., , 2000; and many others, see summary of diesel exhaust particulate pp. 7-13); these adverse immunological effects are not shared by other model particulates such as carbon black and crystalline silica (van Zijverden *et al*., 2000). Additionally, acute exposures of healthy adult humans to concentrations of diesel exhaust particulate matter (300 $\mu g/m^3$) approximately one order of magnitude greater than peak diesel exhaust concentrations noted near California freeways demonstrated a marked leukocytic airway infiltration accompanied by enhanced chemokine and cytokine production (Salvi *et al.*, 2000). It should be noted that 300 $\mu g/m^3$ was a LOEL (Lowest Observable Effect Level) in this study. Lower concentrations of

diesel exhaust particulate matter were not tested, raising the possibility that these effects may be observed at concentrations lower than 300 $\mu g/m^3$. Additionally, Frew *et al.* (2001) observed upregulation of IL-10 production in the bronchial epithelium of asthmatic subjects but not healthy subjects at a PM_{10} concentration of only 108 $\mu g/m^3$. The authors stated that the observed IL-10 upregulation may alter the airway biology towards a more allergic phenotype. It is also possible that healthy and/or asthmatic children may be more sensitive to diesel exhaust particulate matter-induced immune system effects than healthy adults. These data indicate that diesel exhaust particulate matter adversely impacts healthy adult immune systems at concentrations close to those observed in cars driving on California freeways (e.g., up to 23 $\mu g/m^3$), making them very relevant to a consideration of diesel exhaust particulate matter for prioritization under SB 25.

Comment 2: Traffic Density Studies

Several studies are cited that indicate an increase in respiratory symptoms associated with proximity to roadways. It should be pointed out that DEP is only one component of the particulates that are generated by roadway traffic, and in most of the studies cited, it was not even measured. Such studies are also subject to multiple potentially confounding factors. In our previous comments we noted several studies that did not show these traffic related effects. These studies continue to be ignored in this draft. It does not seem useful to either the SRP or the public to present only results that indicate positive effects while leaving out others that show a different outcome. Thus, as a whole, the traffic density line of evidence is also very weak with regard to showing a differential health risk to children. While the data is still forthcoming, some information from the recent OEHHA symposium at UCLA seemed to show that particulate matter from vehicle use (i.e., brake dust, tire wear, re-entrained road dust from other sources) rather than simply DEP could be significantly contributing to asthma in children.

Response 2: This document discusses the uncertainties associated with the adverse health effects reported for the TACs, and includes descriptions of negative studies where appropriate. We considered the studies and comments previously submitted. However, it is not necessary to include a detailed description of every negative study for the prioritized TACs in the literature. Since the purpose of the current review was to identify any potential for differential effects on infants and children, OEHHA concentrated on those studies which contained information on this issue, and did not include in the toxicity summary a number of studies which are uninformative on this point.

The comment points out the difficulty of evaluating epidemiological studies to pinpoint causative agents. However, the statute requires OEHHA to consider multiple pollutant exposures. Therefore, if there is an association between PM_{10} and other co-pollutant and an adverse health effect, that information must still be considered. Most of the studies that looked at respiratory health impacts of traffic-related pollutants specifically looked at truck traffic, which in the countries where the studies were done is all diesel-fueled. Truck traffic density was the metric associated with adverse respiratory health impacts. In addition, one of the studies measured

PM_{10} and soot (largely $PM_{2.5}$) as well as truck traffic density. The strongest correlation with adverse respiratory health impacts in this study (Brunekreef et al, 1996) was with soot, which in these environments is largely from diesel-fueled engines.

It is generally agreed that asthma causation is multifactorial. OEHHA does not state that increased asthma rates in children are due to exposure to diesel exhaust particulate. Rather the evidence from immune toxicity studies of diesel exhaust particulate indicates enhancement of allergic responses even to neoallergens. This, in conjunction with epidemiology studies of asthma exacerbation by particulate air pollution and studies of respiratory health in children living near busy roadways, is reason to believe that diesel exhaust particulate exacerbates asthma and possibly contributes to new asthma cases. OEHHA has also noted in the prioritization document and in its response to comments that no direct epidemiological evidence of differential sensitivity of children to asthma induced specifically by diesel exhaust particulate matter (as opposed to PM_{10} or $PM_{2.5}$) has been published. OEHHA considers asthma to impact children more than adults because of the higher prevalence rates and hospitalizations rates for asthma in children compared to adults. The possibility that diesel exhaust particulate matter may differentially impact children stems from the mechanistic data indicating that diesel exhaust particulate matter exerts specific adverse immune system effects potentially related to asthma and other immune system-related diseases.

Comment 3: General Ambient PM10 Health Effects

As noted in previous comments, many associations have been observed between ambient particulate matter and health effects, but there is little evidence to conclude that DEP is more or less likely to be a causative agent as compared to other components. This is still an active area of research. The information presented by OEHHA would actually lead one to the opposite conclusion. Since the proportion of ambient PM that is composed of DEP varies substantially between cities, and if the effects of PM10 are quantitatively similar across these different cities, this suggests that DEP is not the primary culprit. This does not make a good argument for a differential effect of DEP (as a Toxic Air Contaminant) on children. Particulates as a group are already being reviewed under a separate provision of SB25.

With regard to infant mortality, in our previous comments (both oral and written) we pointed out the article by Lipfert et al. (2000) that discussed geographic confounding in the attribution of PM10 to infant mortality. This very relevant work should be cited in the report (if OEHHA decides to retain the PM10 section of the chapter).

Response 3: There are now a dozen or more studies which evaluated exacerbation of symptoms in asthmatics and air pollution, and hundreds of studies on cardiopulmonary morbidity and mortality associated with exposure to PM_{10}. Many of these studies find a positive association of adverse respiratory and cardiovascular effects with PM_{10}. These studies were done in Europe, the U.S., Mexico, South America, and British Columbia in areas with very different mixes of pollutants. The comment notes that the PM associated adverse health effects have been noted in

a number of cities with differing particulate matter composition, and uses this as a reason to discount the contribution of diesel exhaust particulate to these effects. OEHHA looks at this in quite an opposite light. Since some of the studies which observed an association between PM and asthma, cardiopulmonary morbidity and mortality, and infant mortality were done in cities where the vast majority of particulate was from diesel-fueled engines, then it is extremely difficult to discount a contribution from diesel exhaust particulate to the observed effects. There certainly was not a protective effect in those cities with a large diesel exhaust particulate contribution to PM.

Comment 4: Diesel Particulates Contain PAHs

There is no doubt that diesel particulates contain PAHs, however what is relevant from a toxicological standpoint is the level of dose that would be delivered to target organs. Extractions of high levels of PAH for direct application are of little relevance in answering questions of differential susceptibility to the effects of DEP.

Response 4: The bioavailability of PAHs contained in diesel exhaust was thoroughly reviewed in the diesel exhaust TAC document (OEHHA, 1998). The studies reviewed included occupational exposure studies, and clearly indicated that the PAHs in diesel exhaust were bioavailable upon inhalation exposure. Additionally, a recent study by Sato *et al.* (2000) indicated that rats exposed to diesel exhaust by inhalation demonstrated increased mutations in a reporter gene and covalent DNA adducts, additional evidence suggesting PAH bioavailability. These studies, especially those involving occupational exposures, suggest that the PAH levels present in ambient diesel exhaust particulate matter are toxicologically relevant.

Comment 5: Developmental and Reproductive Effects

The interpretation of the study by Watanabe and Kurita (2001) is incorrect. These authors found the same difference in anogenital distance whether they exposed animals to diesel exhaust or diesel exhaust that had been filtered to remove DEP. The authors concluded that the gaseous phase must have included the relevant toxicants. Furthermore, the exhaust stream contained other compounds associated with combustion as well as products of incomplete combustion. Until one looks at other exhaust streams, (i.e., gasoline, methanol, CNG), it is unclear that the results are due to diesel exhaust and not other components such as NOx.

Furthermore, there is no basis to state on the top of page 26 that it is "plausible" that DEP is a teratogen because PAHs show this effect. There is absolutely no consideration of dose/ response relationships in such a statement. It is also just as plausible that grilled hamburgers and a multitude of other foods are teratogenic using this same logic (since they contain PAHs). Is orange juice a plausible teratogen because it contains ethanol? These statements implying teratogenicity of DEP should be removed from the report.

Response 5: The comment correctly points out that exposure to both unfiltered and filtered diesel exhaust resulted in masculinization of the fetus in Watanabe and Kurita (2001). However, some of the chemicals that might plausibly be associated with this effect (e.g., dioxins, PAHs) exist in the particulate and gaseous phases of the exhaust depending on temperature, dilution processes, and so forth. Until the toxicants responsible for this endocrine effect are identified, it is premature to ascribe the effect solely to the gaseous phase of diesel exhaust.

Diesel exhaust PAHs have been demonstrated to be bioavailable at occupational exposure levels, and PAHs have been demonstrated to have teratogenic effects. The data indicate that it is therefore plausible (i.e., worthy of consideration as a hypothesis) that such effects would also result from exposure to diesel exhaust due to its PAH content. Further, the prioritization document does not state that the available data are sufficient for a determination that diesel exhaust is a teratogen, and acknowledges that "it does not appear that the endpoints observed for PAH developmental toxicity have been adequately evaluated for diesel exhaust exposure".

Response to Comments on Final Public Review Draft Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act

July, 2001

Response to Comments on Methylene Chloride by Paul Dugard (HSIA)

The Halogenated Solvents Industry Alliance (HSIA) submitted comments in response to the notice regarding the prioritization of the Toxic Air Contaminants (TACs) for the California Children's Environmental Health Protection Act (SB25) in a letter from Dr. P.H. Dugard dated July 13, 2001.

Comment 1: Carboxyhemoglobin in the fetus following maternal exposure to methylene chloride could arise from carbon monoxide released by maternal metabolism that reaches the fetal blood, or by metabolism of methylene chloride in fetal tissues. Neither source is likely to contribute to COHb in fetal blood such that the level is above, or even reaches, that in the maternal system.

Response 1: OEHHA agrees that at current ambient levels methylene chloride does not significantly contribute to carboxyhemoglobin levels in fetuses, infants or adults. However, although methylene chloride levels in fetal blood following maternal exposure tend to be lower than those in maternal circulation, carbon monoxide levels in fetal blood do reach levels comparable to maternal blood (Anders & Sunram, 1982). In addition, the fetal capacity to dissociate carboxyhemoglobin and convert CO to CO_2 is lower than in adults.

Comment 2: It should be noted that the metabolism of methylene chloride by P450 enzymes is saturable; this limits the maximum rate of production of carbon monoxide and gives a ceiling to the level of COHb that can occur from exposure to methylene chloride (Andersen et al., 1991). This means that severe carbon monoxide poisoning cannot occur as a result of exposure to methylene chloride.

Response 2: In the experiments reported by Andersen et al (1991) a peak COHb level of 8% was achieved in humans following exposure to methylene chloride at 2,000 ppm for 3 hours. A similar COHb level (9%) was reported by Longo (1970) to be equivalent to a 41% reduction in fetal blood flow or in fetal hemoglobin concentration. Thus while this high level of methylene chloride is unlikely to be encountered except during accidental exposure, this work underscores that for the fetus the consequences of maternal exposure are serious and include not just the formation of fetal COHb, but also a reduction in the oxygen available from maternal circulation. Elevated maternal COHb has been associated with reduced birth weights it humans (Astrup et al., 1972; Longo, 1977), and is thought to contribute to the lower birth weights associated with maternal exposure to methylene chloride during pregnancy in rats (Hardin and Manson, 1980).

Comment 3: None of the factors contributing to the prioritization process, exposure patterns among infants and children that result in disproportionately high exposure; special susceptibility of infants and children; effects of simultaneous exposure to

compounds with the same mechanism of action; any interactions of air pollutants, supports the prioritization of methylene chloride as a Tier 2 substance.

Response 3: The available data suggest that there is a differential susceptibility of children and fetuses to methylene chloride compared to adults. The CO formed after exposure to methylene chloride is bound with greater affinity by fetal hemoglobin, and fetuses and infants are less able to enzymatically eliminate COHb. In addition, the developing fetal nervous system is expected to be more sensitive to hypoxia associated with COHb formation. However, due to its low ambient levels and relatively low toxicity, methylene chloride was not included in Tier 1 and no further action is required or anticipated under this process at this time. Nevertheless, we will keep these comments in mind if future review becomes necessary.

Anders and Sunram. 1982. Transplacental passage of dichloromethane and carbon monoxide. Toxicol Lett 12, 231-4.

Andersen et al. 1991. Physiologically based pharmacokinetic modeling with dichloromethane, its metabolite, carbon monoxide, and blood carboxyhemoglobin in rats and humans. Toxicol Appl Pharmacol 108, 14-27.

Astrup et al. 1972. Effect of moderate carbon-monoxide exposure on fetal development. Lancet 2, 1220-2.

Hardin and Manson. 1980. Absence of dichloromethane teratogenicity with inhalation exposure in rats. Toxicol Appl Pharmacol 52, 22-8.

Longo. 1970. Carbon monoxide in the pregnant mother and fetus and its exchange across the placenta. Ann NY Acad Sci 174, 312-41.

Longo. 1977. The biological effects of carbon monoxide on the pregnant woman, fetus, and newborn infant. Am J Obstet Gynecol 129, 69-103.

Response to Comments on Final Public Review Draft Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act

July, 2001

Responses to Comments on Diesel Particulate Submitted by American Trucking Association

Comment 1: OEHHA has not Provided Interested Parties with Adequate Time in which to Comment on the Revised Listing.

As a preliminary matter, we note that notice concerning OEHHA's decision to revise the prioritization of TACs under the Children's Environmental Health Protection Act was not posted on OEHHA's website until June 29, 2001, leaving stakeholders with a very generous comment period of 2 weeks (which includes 2 weekends and the Fourth of July holiday). This abbreviated comment period is inadequate to prepare comprehensive comments on such a complex subject. As a result, ATA and other interested stakeholders have been denied a reasonable opportunity to offer detailed comments on the decision to replace benzene and formaldehyde with diesel exhaust particulate and acrolein as Tier 1 substances under the Children's Environmental Health Protection Act.

ATA recognizes that the statutory deadline for this listing passed on July 1, 2001; however, the reshuffling of listed chemicals immediately prior to the statutory deadline without an adequate opportunity to receive meaningful public comment is a clear violation of administrative procedure that will not withstand judicial scrutiny.[1] To cure this procedural defect, OEHHA should publish a formal extension to the comment period and allow interested parties an opportunity to supplement the record.

Response 1: The comment indicates that there was little time to comment on the revised prioritization. It must be noted that the same arguments that diesel exhaust particulate may cause infants and children to be especially susceptible to illness were made in the initial and latest versions of the prioritization document. In the initial and later versions, it was made clear in the text of the document that the prioritization into the top Tier of 5 TACs for listing under Health and Safety Code Section 39669.5 was subject to public and peer review comments. Thus, interested parties knew that it was quite possible any of the chemicals discussed in the document could end up in the final five proposed for listing under SB 25. The initial draft of the prioritization document was posted on March 7th for a 30-day comment period (ATA provided comments then). The document was open for comment during the Panel deliberations (which started officially at the first SRP meeting on the subject held on April 27th). At the Scientific Review Panel Meeting June 15th, the SRP provisionally approved OEHHA's suggested revisions to the prioritization document and Tiers 1 and 2 pending a final public comment period on the document. We discussed in the record when that public comment period would start and end. In attendance at that public meeting was legal representation for the Engine Manufacturers Association, an organization with which ATA is in close communication. Furthermore, the revised

[1] *See* Cal. Gov't Code Sections 11346.4, 11346.8.

document was posted on our webpage along with the notice of the public comment period on June 23rd. Thus, there was a longer period of time to develop comments than the comment indicates. Furthermore, no new lines of evidence were brought forth in the final document as regards diesel exhaust particulate and potential differential impacts on infants and children, and no new issues are being raised by ATA; therefore, it is unclear why the commenter needs more time.

As the comment notes, there was a very tight timeline for this entire process.

Comment 2: OEHHA Should Delay Listing Diesel Exhaust Particulate Matter as a Tier 1 Substance in Light of Pending Litigation.

In our initial comments, we noted that the listing of diesel exhaust as a TAC in the State of California currently is the subject of litigation.[2] This litigation questions whether the classification of diesel exhaust particulate matter as a TAC is supported adequately by scientific evidence. The legal challenge to the diesel exhaust particulate matter TAC listing already has withstood the government's demurrer, with Judge Stephen Kane having ruled that the suit alleges valid causes of action. The case now will be heard on the merits. Accordingly, it is inappropriate to list diesel particulate as a Tier 1 substance until the litigation concludes.

Response 2: There is no reason to delay listing under SB 25. Diesel exhaust particulate is an identified toxic air contaminant and therefore subject to consideration for listing under SB 25.

Comment 3: OEHHA'S Basis for Listing Diesel Particulate Matter in Tier 1 is Unsupported by the Scientific Evidence in the Record.

OEHHA erroneously included diesel exhaust among the five Tier 1 TACs that disproportionately impact children. OEHHA sets forth the following reasons for including diesel exhaust particulate in Tier 1:

[D]iesel exhaust particulate is ubiquitous in urban environments, and exposures are widespread. There are many studies demonstrating that diesel exhaust particulate can enhance allergic responses, and induce new allergies to airborne allergens. This raises concern for enhancement of allergic airway

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[2] *See Apodaca v. California Air Resources Board*, (Superior Court Case No. 00CECG10832).

disease including asthma, and for development of new asthma. Diesel exhaust particles contribute to ambient PM10. Ambient PM10 has been shown to exacerbate asthma and has been associated with low birth weight and decreased lung function in children. In addition, diesel exhaust particulate contains PAHs [polycyclic aromatic hydrocarbons] (and other mutagenic polycyclic organic matter).[3]

The above paragraph indicates that OEHHA's decision to elevate diesel exhaust particulate matter to Tier 1 is based upon the following three observations:

Diesel exhaust particles contribute to ambient PM_{10};
Diesel exhaust particles contain PAH; and
Diesel exhaust particulate may exacerbate asthma and enhance allergic responses.

As demonstrated in these comments and the initial comments submitted by the ATA, these observations and the inconclusive science they are based upon are insufficient to support a conclusion that diesel exhaust "may cause children and infants to be especially susceptible to illness."

Comment 3a: Diesel Exhaust is a small contributor to ambient particulate matter.

OEHHA's statement that diesel exhaust particulate is ubiquitous in urban environments and contributes to ambient particulate matter, overstates the impact diesel exhaust has upon ambient particulate matter. Diesel exhaust is a very small component of PM_{10}. Recent EPA national assessment data reports diesel exhaust (from both on-road and non-road sources) contributed only 1.3% of total emitted PM_{10} and 4.9% of total emitted $PM_{2.5}$. Thus, it is misleading to characterize diesel exhaust as a significant source of ambient particulate matter.

Even if one could completely eliminate diesel exhaust from the ambient air, the impact of particulate matter upon infants and children likely would remain. As such, control of diesel exhaust as a separate air contaminant will not solve the problem of exposure to ambient particulate matter, which already receives adequate regulatory attention as a criteria pollutant for which levels are set to protect the health of sensitive populations such as infants and children. OEHHA should focus its attention on air toxics for which additional regulation will result in tangible health benefits for infants and children.

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[3] Office of Environmental Health Hazard Assessment California Protection Agency "Prioritization of Toxic Air Contaminants Under the Children's Environment Health Protection Act" Final Public Review Draft, p. 35 (June 2001).

Response 3a: As stated in the diesel exhaust SB25 prioritization data summary document, based on the ARB 1990 emissions inventory, approximately 58,000 tons of diesel exhaust PM_{10} from all sources are emitted into California air each year (ARB, 1997). ARB staff have estimated that emissions from diesel exhaust contribute about 3 and 8 percent of the total California PM_{10} and $PM_{2.5}$ inventories, respectively (ARB, 1997). This is averaged over all sources and therefore is not reflective of the percentage of PM_{10} or $_{2.5}$ that is diesel exhaust particulate in areas with heavy traffic (e.g., near freeways and in highly urbanized areas). The statewide population-weighted average diesel exhaust PM concentration is estimated to be 3.2 $\mu g/m^3$. An ARB study to determine the PM_{10} concentrations due to the primary emissions from diesel engine exhaust near the Long Beach Freeway indicated that near-roadway concentrations of diesel exhaust PM_{10} may be as high as 8 $\mu g/m^3$ above ambient concentrations for one 24-hour period (ARB, 1996). This is notable in light of the fact that the chronic Reference Exposure Level (REL) for diesel exhaust is 5 $\mu g/m^3$. In addition, measurements conducted by ARB in vehicles on Los Angeles freeways indicated concentrations of black soot up to 23 $\mu g/m^3$, which were strongly influenced by presence of diesel vehicles in front of the test vehicle. After considering these facts along with the cancer and noncancer health effects data for diesel exhaust, it is clear that diesel exhaust is in fact an important source of air pollutants. The exposure assessment section of the diesel TAC identification document also observes:

> "These total exposures estimates are believed to underestimate, to an unknown extent, Californians' actual exposures to diesel exhaust particles. This is because insufficient data are available for concentrations inside vehicles and along roadways to allow such near-source, elevated exposures to be estimated for the population". (ARB, 1998, page A-57)

Zelinska (1991, cited by ARB, 1998) found that motor vehicle exhaust was the second highest contributor to wintertime PM_{10}, and that diesel-fueled motor vehicle exhaust was responsible for at least half of the motor vehicle derived PM_{10}. Also, as described by ARB (1998), PAHs are generally associated with the particles composed of elemental carbon (EC), rather than the mineral particles of geological or atmospheric origin. ARB found that

> "… diesel emissions were responsible for approximately 67 percent of the fine EC mass in the Los Angeles atmosphere, and that the exhaust particles averaged about 64 percent EC." (ARB, 1998, page A-47)

The document does not state that diesel exhaust is a significant source of PM for the entire state of California. It does state that "Although the contribution of diesel exhaust particulate to the statewide average PM_{10} is relatively small in California (5% or so), it is a more significant portion of PM_{10} and $PM_{2.5}$ in urban locations". It should also be noted that diesel exhaust particulate causes adverse immune system effects, which may result in

adverse health outcomes (e.g. possible exacerbation of asthma and allergic rhinitis) (Diaz-Sanchez *et al*., 2000), that are not shared by other model particulates such as carbon black and crystalline silica (van Zijverden et al., 2000). This suggests that diesel exhaust particulate has additional unique toxicological properties above and beyond the cardiopulmonary morbidity and mortality associated with exposure to general ambient PM_{10}.

Comment 3b: Diesel Exhaust Particulate's Polycyclic Aromatic Hydrocarbon Content does Not Justify the Listing of Diesel Exhaust as Potentially Having a Disproportionate Impact Upon Children.

OEHHA reasons that "diesel exhaust particulate contains PAHs." In fact, OEHHA has not actually quantified the contribution of diesel exhaust particulate matter to ambient PAH. More importantly, OEHHA will list PAHs independently among the Tier 1 substances. Therefore, to the extent that PAHs contained in diesel exhaust may cause children and infants to be especially susceptible to illness, these impacts would be addressed following the finalization of PAHs on the Tier 1 list. A separate listing for diesel exhaust particulate matter based partly upon the presence of PAHs is unwarranted.

As highlighted in our original comments, OEHHA has not investigated whether the diesel exhaust particles bind or release PAHs in the presence of bodily fluids. Prior to listing diesel exhaust as a contaminant that may disproportionately impact the health of children based upon its PAH content, it is important to know whether PAHs are absorbed into the body. It is theoretically possible for PAHs to remain bound to diesel exhaust particulates, thereby having no adverse health effect once absorbed into the body. OEHHA cites to no studies attempting to describe how the body metabolizes diesel exhaust. In the absence of such evidence, the mere presence of PAHs in diesel exhaust is insufficient to form a conclusion of adverse health effects.

Response 3b: It is well documented that all the physical phases of diesel exhaust contain PAHs, and contribute to ambient PAHs. An exact quantification of the contribution of diesel exhaust particulate matter to total ambient PAH is not a necessary requirement for listing diesel exhaust in Tier I. The bioavailability of PAHs contained in diesel exhaust was thoroughly reviewed in the diesel exhaust TAC document (OEHHA, 1998). The studies reviewed clearly indicated that the PAHs in diesel exhaust were bioavailable upon inhalation exposure. Additionally, a recent study by Sato *et al.* (2000) indicated that rats exposed to diesel exhaust by inhalation demonstrated increased mutations in a reporter gene and covalent DNA adducts, additional evidence suggesting PAH bioavailability. However, the presence of PAHs in diesel exhaust was not the sole reason for the listing of diesel exhaust in Tier I of the prioritization document.

Mechanistic data indicates that diesel exhaust particulate matter may exert specific effects on the immune system that are not shared by some other PM components such as crystalline silica (van Zijverden *et al.*, 2000). Additionally, diesel exhaust has immune system effects not necessarily shared by other model particulates such as carbon black (Diaz-Sanchez *et al.*, 2000). Some of these effects, such as enhancing ovalbumin-induced IgG1 and IgE levels in mice were also shown by extracts of DEPM and the polycyclic aromatic hydrocarbons (PAHs) phenanthrene and anthracene (Heo *et al.*, 2001). However, these same effects were not shown by the PAHs 3-methylcholanthrene and acenaphthylene or by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), suggesting that the effects may not be globally attributable to either all PAHs or *Ah* receptor ligands. This indicates that non-PAH components of diesel exhaust could potentially also be exerting adverse immune system effects, in addition to other adverse health effects associated with PM exposure.

Comment 3c: Diesel exhaust particulate can exacerbate asthma and enhance allergic responses.

As stated in our original comments, OEHHA states that diesel exhaust contributes to ambient particulate matter and then notes that ambient particulate matter has been shown to exacerbate asthma and has been associated with low birth weight and decreased lung function. Based upon this evidence, OEHHA concludes that diesel exhaust, as a component of particulate matter, is a substance of concern. However, OEHHA cites no scientific evidence directly linking diesel exhaust to these adverse effects or demonstrating that exposure to diesel exhaust triggers an adverse health effect different from exposure to particulate matter generally.[4]

The available studies that measure the effect on children of diesel exhaust exposure are limited, both in number and in design. The studies that measure the non-cancerous effects of diesel exhaust exposure in adults, however, consistently show no effect or only acute transient effect on respiratory status. The available studies, therefore, do not provide a basis to conclude that diesel particulate matter places children at a greater risk for non-cancerous respiratory illness. Additionally, the ambient particulate matter levels that may contribute to respiratory illnesses are comprised of various emission sources, of which diesel exhaust is a small fraction. Current regulations have reduced, and will continue to reduce diesel exhaust emissions.

Response 3c: There are a number of studies demonstrating adverse health impacts in infants and children from exposure to PM_{10} in ambient air. The adverse health outcomes measured range from exacerbation of asthma symptoms to infant and child mortality.

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[4] *See* ATA's Initial Comments, Section III.B.2.a, attached hereto as Appendix A.

These studies took place in a number of cities with varying percentage of total PM_{10} that is diesel exhaust particulate. However, in some of the cities studied, diesel exhaust particulate contributes the vast majority of PM_{10}. There was certainly no protective effect of diesel exhaust particulate in these studies. It is therefore reasonable to conclude that diesel exhaust particulate as a component of airborne PM_{10} has the adverse effects attributable to airborne PM_{10}.

There are several dozen studies demonstrating enhancement of allergic responses in both humans and animals following exposure to diesel exhaust particulate. As noted in the response to Comment 3b, diesel exhaust particulate causes adverse immune system effects that may result in adverse health outcomes (e.g. possible exacerbation of asthma and allergic rhinitis) (Diaz-Sanchez *et al*., 2000, and others; see diesel exhaust summary pp. 7-13); these adverse immunological effects are not shared by other model particulates such as carbon black and crystalline silica (van Zijverden *et al*., 2000). This suggests that diesel exhaust exhibits noncancer health effects that are unique over and above the cardiopulmonary morbidity and mortality associated with exposure to ambient general particulate matter. Acute exposures of healthy adult humans to concentrations of diesel exhaust particulate matter (300 $\mu g/m^3$) approximately one order of magnitude greater than peak diesel exhaust concentrations noted near California freeways demonstrated a marked leukocytic airway infiltration accompanied by enhanced chemokine and cytokine production (Salvi *et al.*, 2000). It should be noted that 300 $\mu g/m^3$ was a LOEL (Lowest Observable Effect Level) in this study. Lower concentrations of diesel exhaust particulate matter were not tested, raising the possibility that these effects may be observed at concentrations lower than 300 $\mu g/m^3$. Additionally, Frew *et al.* (2001) observed upregulation of IL-10 production in the bronchial epithelium of asthmatic subjects but not healthy subjects at a PM_{10} concentration of only 108 $\mu g/m^3$. The authors stated that the observed IL-10 upregulation may alter the airway biology towards a more allergic phenotype. It is also possible that healthy and/or asthmatic children may be more sensitive to diesel exhaust particulate matter-induced immune system effects than healthy adults. These data indicate that diesel exhaust particulate matter adversely impacts healthy and asthmatic adult immune systems at concentrations close to those observed in cars driving on California freeways (e.g., about 25 $\mu g/m^3$), making them very relevant to a consideration of diesel exhaust particulate matter for prioritization under SB 25.

Comment 3d: **Replacing Diesel Exhaust Particulate in Place of Benzene and Formaldehyde is Contrary to the Statutory Listing Criteria Under the Children's Environmental Health Protection Act.**

The last minute substitution of diesel particulate matter in place of a substance such as benzene defies logic and cannot be justified under the statutory criteria established by the Children's Environmental Health Protection Act. Most significantly,

benzene is a known carcinogen, whereas diesel particulate is suspected of aggravating respiratory conditions such as asthma.

No scientific studies substantiate OEHHA's conclusion that diesel exhaust particulate enhances allergic responses, induces new allergies to airborne allergens, and may enhance allergic airway disease. The published literature on diesel particulate matter suggest that at high concentrations, the PAHs adsorbed to diesel particulate matter *may* act as an adjuvant to enhance allergic responses in people already pre-sensitized to an allergen when co-administered with an allergen. There is no, and the OEHHA does not cite to, scientific evidence that diesel exhaust particulate enhances allergic airway disease. Available studies performed on volunteers directly exposed to diesel exhaust under experimental laboratory conditions show at most only transient effects of diesel exhaust on respiratory function. There are no human exposure or epidemiological studies that show diesel exhaust exposure causes chronic respiratory disease.

The most recent studies characterize the soluble organic chemical portion of diesel particulate matter as the adjuvant, not the actual carbon particle. Exposure to carbon particle alone in a murine model induced no immuno-adjuvant effect. The soluble organic chemical agents on the carbon black particle include PAHs and other chemicals. As stated previously, PAHs already are listed as a Tier 1 pollutant. It therefore makes no logical sense to remove benzene from Tier 1 in order to elevate the importance of diesel particulate, when the scientific evidence suggests the only component of diesel exhaust particulate that causes any appreciable health effect is already addressed as a Tier 1 pollutant.

Response 3d: Diesel exhaust particulate has been one of the candidates for listing under SB 25 since the beginning of this process and was listed as a candidate in the initial draft of the document. Thus, the comment's statement that diesel exhaust particulate was a last minute substitution for benzene is a bit misleading. There were 12 top candidates in the initial draft of the document which clearly stated in several places that the placement of the chemicals into two Tiers was subject to public and peer review comment. In addition, the first paragraph of the comment indicates that while benzene is a carcinogen, diesel exhaust particulate only exacerbates asthma. The Toxic Air Contaminant (TAC) document for Particulate Matter From Diesel-Fueled Engines (OEHHA, 1999) discussed in detail the more than 3 dozen studies showing elevated risks for lung cancer in diesel exhaust exposed workers. The TAC Identification document for diesel describes the development of a cancer unit risk value range for diesel exhaust, and states "a reasonable and likely explanation for the increased risks of lung cancer observed in the epidemiologic studies is a causal association between diesel exhaust exposure and lung cancer". Diesel exhaust exposure carries a cancer risk in addition to non-cancer toxic effects, including possible exacerbation of asthma. Diesel exhaust is also regulated as a carcinogen by the Occupational Safety and Health Administration; the International Agency for Research on Cancer classifies diesel exhaust as a 2A carcinogen.

There are several dozen studies which provide evidence that diesel exhaust particulate enhances allergic responses to allergens and even to neo allergens in both humans and animals (see Diesel exhaust particulate summary, pp.7-13). As noted in the responses to Comments 3a, b and c, diesel exhaust particulate demonstrates immune system effects (which may result in adverse health outcomes such as exacerbation of asthma and allergic rhinitis) (Diaz-Sanchez *et al*., 2000) that are not shared by other model particulates such as carbon black and crystalline silica (van Zijverden *et al*., 2000). This suggests that diesel exhaust exhibits noncancer health effects that are unique over and above the cardiopulmonary toxic effects of exposure to ambient general particulate matter. Some of these effects, such as enhancing ovalbumin-induced IgG1 and IgE levels in mice were also shown by extracts of DEPM and the polycyclic aromatic hydrocarbons (PAHs) phenanthrene and anthracene (Heo *et al.*, 2001). However, these same effects were not shown by the PAHs 3-methylcholanthrene and acenaphthylene or by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), suggesting that the effects may not be globally attributable to either all PAHs or *Ah* receptor ligands. This indicates that non-PAH components of diesel exhaust could potentially also be exerting adverse immune system effects, in addition to other adverse health effects associated with PM exposure.

Acute healthy adult human exposures to concentrations of diesel exhaust particulate matter (300 $\mu g/m^3$) approximately one order of magnitude greater than peak diesel exhaust concentrations noted near California freeways demonstrated a marked leukocytic airway infiltration accompanied by enhanced chemokine and cytokine production (Salvi *et al.*, 2000). This represents an allergic inflammatory reaction. It should be noted that 300 $\mu g/m^3$ was a LOEL (Lowest Observable Effect Level) in this study. Lower concentrations of diesel exhaust particulate matter were not tested, raising the possibility that these effects may be observed at concentrations lower than 300 $\mu g/m^3$. Additionally, Frew *et al.* (2001) observed upregulation of IL-10 production in the bronchial epithelium of asthmatic subjects but not healthy subjects at a PM_{10} concentration of only 108 $\mu g/m^3$. The authors stated that the observed IL-10 upregulation may alter the airway biology towards a more allergic phenotype. It is also possible that healthy and/or asthmatic children may be more sensitive to diesel exhaust particulate matter-induced immune system effects than healthy adults. These data indicate that diesel exhaust particulate matter adversely impacts healthy adult immune systems at concentrations close to those observed near California freeways, making them very relevant to a consideration of diesel exhaust particulate matter for prioritization under SB 25.

The comment also appears to imply that the only toxic constituent of diesel exhaust particles are the PAHs which may be actors in the observed enhancement of allergy in humans and animals. While there is a line of evidence that indicates PAHs are involved in this response, it is by no means clear that they are the only chemicals absorbed to the carbon core that influence the allergic inflammatory responses observed.

OEHHA has also noted in the prioritization document and in its response to comments that no direct epidemiological evidence of differential sensitivity of children to asthma induced specifically by diesel exhaust particulate matter (as opposed to PM_{10} or $PM_{2.5}$) has been published. OEHHA considers asthma to impact children more than adults primarily because children have higher prevalence rates for asthma and are hospitalized more often than adults for asthma. The possibility that diesel exhaust particulate matter may differentially impact children stems from the mechanistic data indicating that diesel exhaust particulate matter exerts specific adverse immune system effects. The adverse health effects observed in the traffic studies cited in the document, as well as the epidemiological studies observing a positive correlation between PM_{10} and exacerbation of asthma, provide additional support for the conclusion that diesel exhaust particulate may exacerbate asthma.

Responses to Comments on Ethylene Glycol Ethers by the American Chemistry Council

Comments by the Ethylene Glycol Ethers Panel of the American Chemistry Council (ACC) were received in a letter dated July 12, 2001 from Susan A. Lewis, Ph.D., Ethylene Glycol Ethers Panel Manager. (In a earlier letter (dated March 28,2001), the Panel urged OEHHA to delete ethylene glycol methyl ether (EGME), ethylene glycol ethyl ether (EGEE), and their acetates (EGMEA and EGEEA) from its list of priority candidates).

Comment 1. In the table on page 38 of the summary document, the current reference to "Glycol Ethers (EE and ME but not BE)" should be replaced by "EGME, EGEE, EGMEA and EGEEA."

Response 1. The reference has been changed to Ethylene Glycol Ethers (EGEE, EGME, EGEEA, and EGMEA).

Comment 2. In the Appendix C-2 chemical toxicity summary for these compounds, the title should be changed from "Ethylene Glycol Ethers" to "EGME, EGEE, EGMEA and EGEEA," reflecting the fact the summary only discusses these four ethylene glycol ethers.

Response 2. The title has been changed to "Ethylene Glycol Ethers (EGME, EGEE, EGMEA, EGEEA)."

The Toxic Air Contaminant Identification List Summaries, which were released by the ARB in September 1997, state: "Glycol ethers, as defined in the federal Clean Air Act Section 112(b) and listed as "Must Be Quantified for Emissions Inventory" for the Air Toxics "Hot Spots" Program (AB 2588), are diethylene glycol dimethyl ether, diethylene glycol monobutyl ether, diethylene glycol monoethyl ether, diethylene glycol monomethyl ether, ethylene glycol diethyl ether, ethylene glycol dimethyl ether, ethylene glycol monobutyl ether, ethylene glycol monoethyl ether, ethylene glycol monoethyl ether acetate, ethylene glycol monomethyl ether, ethylene glycol monomethyl ether acetate, ethylene glycol monopropyl ether, and triethylene glycol dimethyl ether." This statement is based on the actual wording of the listing for glycol ethers as Toxic Air Contaminants: "Glycol ethers: Includes mono- and di-ethers of ethylene glycol, diethylene glycol, and triethylene glycol (R(OCH2CH2)n -OR' where n = 1,2 or 3 R = alkyl or aryl groups R' = R,H, or groups which, when removed, yield glycol ethers with the structure; R(OCH2CH)n-OH. Polymers are excluded from the glycol category." ARB also stated: "Currently, the inclusion of propylene glycol ethers in the definition of glycol ethers is being debated within the United States Environmental Protection Agency (U.S. EPA), but no decisions have been made."

Thus although EGEE, EGEEA, EGME, and EGMEA are the glycol ethers of most concern (and some of the most thoroughly studied), OEHHA does not have the authority to ignore other glycol ethers which are listed. OEHHA staff are concerned that some portion of the unspeciated 2,922,744 pounds of Hot Spots glycol ether emissions may be comprised of EGME, EGEE, EGMEA and EGEEA. Even if none of the unspeciated emissions were of those four glycol ethers, those emitted are still likely to be listed Toxic Air Contaminants.

Response to Comments Submitted by International Truck and Engine

Comment I: OEHHA Has Failed to Develop Uniform Criteria for Listing Tier 1 TACs, Resulting in Inconsistent Treatment of TACs.

Comment Ia: Although OEHHA points to five criteria in its Prioritization as its "guide" in selecting the Tier 1 TACs,[1] OEHHA fails to provide any explanation as to how they have interpreted these criteria, and even more worrisome, fails to establish a method of weighing various risk factors against each other (*e.g*. severe effects with a potentially lesser exposed population versus less severe effects with a potentially greater exposed population). Asked whether a TAC that exacerbates asthma or one that causes neural, developmental impairment would get a higher listing, Dr. Melanie Marty, Chief Air Toxicologist at OEHHA responded, "if I had my choice, I think I'd rather have asthma than developmental neurotoxicity. I mean, that's about all you can do to weigh that kind of an issue."[2] Yet without a specific, clear methodology for conducting a comparative analysis of the candidate TACs, the process has become haphazard and non-transparent, with inconsistent outcomes.

Response Ia: In the Introduction section of the document, we describe the methods used to prioritize the TACs for evaluation for listing under SB 25. We began with the entire list of over 200 TACs and prioritized them based on estimates of potency and/or noncancer Reference Exposure Levels coupled with measurements or estimates of typical ambient air concentrations. Thus, both considerations of exposure, as required by the statute, and considerations of toxic potency were utilized in prioritizing the chemicals. A high noncancer hazard quotient (ratio of the ambient air concentration to the Reference Exposure Level) or a high cancer risk estimate (product of the unit risk factor and the ambient concentration) would suggest further review. Because many of the RELs and potency factors do not specifically account for differential effects in children, we also evaluated whether the TACs impact specific target organs or have other

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[1] OEHHA states that it will use the following criteria as a guide to selecting the Tier 1 TACs: (1) any evidence indicating that infants and children may be more susceptible than adults to the toxicological effects associated with that TAC; (2) the nature and severity of the effect(s), especially irreversible effects; (3) any evidence indicating that, based on current risk assessment methodology, the existing health criteria may not be adequately protective of infants and children; (4) any potential difference in susceptibility of infants and children relative to adults to carcinogenesis based on known information or plausible mechanisms; and (5) extent of exposure and/or the magnitude of risk estimated to occur at concentrations typical of California urban ambient air, and any indication that infants and children may be more heavily exposed to materials contaminated by airborne particles. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, *Prioritization of Toxic Air Contaminants Under the Children's Environmental Health Protection Act*. p. 9-10 (June 2001).

[2] Transcript of the Meeting of the Scientific Review Panel on Toxic Air Contaminants at 139-140 (April 27, 2001).

specific toxic effects (e.g., developmental toxicity, exacerbation or induction of asthma) that would have greater impacts in infants and children than adults. The toxicological endpoints of greater concern were neurotoxicity, immunotoxicity, endocrine toxicity, and respiratory toxicity. Concern for these endpoints stems from the relatively long period of development of these organ systems (e.g., up through adolescence), and the potential for prolonged effects from early chemical insult.

We also examined emissions inventory data from the Air Toxics Hot Spots program to estimate the extent of emissions from stationary sources, which gives an indication of whether localized high concentrations might be encountered near sources. Such localized exposures are not reflected in general ambient air monitoring.

Based on all these considerations, thirty-six TACs were selected for focused literature review, while others were deferred to future evaluations. The comment implies the process was non-transparent and haphazard. That is certainly not the case. The comment points out the difficulty of comparing one toxicological endpoint with another, which was discussed at the SRP meetings. Since all chemicals do not act in exactly the same way on the same target organs, then such comparisons are innate in any prioritization and must be done to the best of our ability. We believe we have done just that. We have looked at the entirety of the available information on whether a chemical might cause infants and children to be especially susceptible to illness for each TAC in prioritizing for listing. This was not a haphazard process and is fully explained in the document (see pp. 5-39).

Comment Ib: In these comments, we provide just a few examples of the problems resulting from OEHHA's haphazard evaluation of the candidate TACs. First, OEHHA's criteria requires it to consider "the nature and severity of the effect(s), especially irreversible effects" in the development of its Tier 1 list.[3] It seems obvious that a TAC whose primary impact on children is carcinogenic should be ranked higher than a TAC whose primary effect on children is non-cancerous. In some cases, but not in others, OEHHA appears to follow this general principle. For instance, OEHHA has listed PCBs in Tier 1 due to their "developmental toxicity, effects on the immune system, endocrine system, and carcinogenicity," despite the fact that they have been banned for several years.[4] Severity trumped low exposure.

Yet OEHHA has inconsistently applied the same criteria to benzene and diesel particulate. Benzene, which is *known* to cause a cancer (leukemia) that is on the rise in children, has been removed from Tier 1. In contrast, diesel particulate, which is *alleged* to induce or exacerbate asthma, has been elevated to Tier 1. OEHHA's treatment of these two chemicals cannot be reconciled by any logical or scientific means – nor can it

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[3] *Prioritization* at 9.

[4] *Id.* at 35.

be squared with a statutory mandate to identify those TACs which pose the greatest risk to children.

Not only is benzene *known* to cause leukemia (among other cancers)[5]; the U.S. EPA has found that the cancer risk from current benzene exposures exceeds 100 in a million for tens of thousands of people. Over a *hundred million people* are exposed to levels of benzene that exceed a 10 in a million risk of cancer and *every single person in the entire U.S. population, including every child, is exposed to a level of benzene that exceeds a one in a million risk of cancer*.[6] In addition to this evidence of the widespread risks of benzene exposure, U.S. EPA has specifically found that there is a "greater risk of leukemia and other toxic effects to children if they are exposed to benzene at similar levels as adults."[7] Moreover, both human and animal data support an association between maternal and paternal exposure to benzene and an increased incidence of leukemia in children.[8] OEHHA, however, removed benzene from Tier 1 because some other epidemiological studies did not find an association between paternal benzene exposure and an increased incidence of leukemia in children, leading OEHHA and the Scientific Review Panel ("SRP") to conclude that the evidence of differential effects in children is only "suggestive."[9]

In contrast, diesel particulate is *not* a known carcinogen and has not been included in the Prioritization based on cancer. Rather, diesel particulate is listed primarily because of preliminary evidence indicating a potential linkage between exposure to diesel particulate and inducement or exacerbation of asthma. As is discussed in more detail below, however, the data cited by OEHHA is incomplete and inconclusive. Moreover, there is *absolutely no scientific evidence* to support a conclusion that diesel particulate has any differential effects in children – even assuming diesel particulate does induce or exacerbate asthma. In short, benzene causes a more severe effect (leukemia) and one

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5 Benzene has been classified as a "known human carcinogen" (category A) under the EPA's Risk Assessment Guidelines of 1986 and causes leukemia, among other cancers. U.S. EPA. Iris Substance file – Benzene. II.A.1. (January 19, 2000), *available at* http://www.epa.gov/iris/subst/0276.htm. Under the proposed revised Carcinogen Risk Assessment Guidelines, benzene is also characterized as a known human carcinogen for all routes of exposure based upon convincing human evidence as well as supporting evidence from animal studies. *Id.*

6 EPA Office of Air Quality Planning and Standards. *Draft National-Scale Air Toxics Assessment for 1996,* Figure 5-2. 1996 Risk Characterization: Population whose 1996 exposure exceeded set cancer risk levels based on all source sectors and background. (January 18, 2001).

7 EPA. National Center for Environmental Assessment. *Carcinogenic Effects of Benzene: An Update.* p. 41 (April 1998).

8 *Prioritization* at Appendix C-2, Benzene – 5-10; 17.

9 *Id.* Benzene – 19.

which is on the rise in children, benzene exposures exceed acceptable risk levels for every member of the population (including all children), and benzene has been shown in some scientific studies to have a differential (greater) effect on children. Yet benzene has been moved to Tier 2. In contrast, there is preliminary evidence that diesel exhaust may induce or exacerbate a less severe condition (asthma) – although likely not at ambient exposure levels – and there is *no* scientific evidence of a differential effect on children, yet it has been moved to Tier 1. OEHHA's inconsistent treatment of these two chemicals simply cannot be squared with its statutory mandate and requirement to engage in reasoned decision making.

Response IB: The comment implies that carcinogenic effects in children should be ranked higher than non-cancerous effects in children. The law requires that we look at TACs to determine which "may cause infants and children to be especially susceptible to illness". A chemical that is a carcinogen may or may not be more potent in children than adults. Similarly, noncancer toxicological endpoints may or may not be more severe in children than adults. Thus, the comment's implication that all carcinogens should be listed first seems misplaced.

The comment correctly points out that severity of effects is a concern and points to the recommendation to list PCBs as following this principle. The implication is that diesel exhaust particulate matter does not have severe effects. OEHHA considers adverse respiratory health impacts, including exacerbation of asthma in young children, to be severe effects. In addition, this comment fails to point out that diesel exhaust particulate matter is carcinogenic. The comment goes on to describe the cancer risk from benzene as a serious concern. We agree that the cancer risk from benzene exposure should be minimized to the extent practicable. However, diesel exhaust particulate matter is a lung carcinogen and the estimated cancer risks from diesel exhaust in urban ambient air may far exceed the cancer risks from benzene in urban ambient air (by well over an order of magnitude; see South Coast AQMD MATES report). The comment stresses that benzene is a known carcinogen but implies that diesel exhaust particulate matter is not. In evaluating diesel exhaust particulate matter as a TAC, the OEHHA health effects evaluation focused on the more than 3 dozen studies indicating excess risk of lung cancer in occupationally exposed workers. OEHHA concluded that a likely and reasonable explanation for the elevated risk of lung cancer in these occupational cohorts is exposure to diesel exhaust as confounders could not explain the elevated risks. Thus, the epidemiological evidence indicates that diesel exhaust particulate matter is associated with lung cancer in humans.

The comment makes a good point that benzene is a leukemogen. OEHHA remains concerned that since leukemia is the most common form of childhood cancer, we should be very cautious about benzene exposures to children. Thus, while there are a number of pieces of evidence that contribute to the concern that benzene exposure might be worse in children than adults, the epidemiological evidence to date does not strongly support a higher risk of leukemia from benzene exposure of children (or their parents)

relative to adults. We thus decided that, for this first listing of TACs, we would not place benzene in the first five. This is not the same thing as having no concern over benzene exposures.

Comment Ic: OEHHA's subjective process also has resulted in diesel particulate being treated inconsistently as compared to formaldehyde. Krzyzanowski, et al. (1990) directly compared the differential respiratory effects of formaldehyde exposure in children versus adults. Despite Krzyzanowski's findings that children's lung function was impacted when exposed to low levels of formaldehyde (while adults were not so impacted), OEHHA moved formaldehyde to Tier 2 – while elevating diesel particulate, for which there is *no* evidence to suggest a differential impact in children. OEHHA's reluctance to associate formaldehyde with inducement or exacerbation of asthma in children is also perplexing given the extensive epidemiological evidence of formaldehyde induced-asthma.[10] Indeed, the National Academy of Sciences itself has identified evidence demonstrating a *differential* impact in children, noting "acute changes in children, especially asthmatics, who were specifically exposed [to formaldehyde] overnight in their bedrooms; morning PEF had decreased significantly with a demonstrable exposure-response relationship."[11]

Similarly troubling is OEHHA's decision to focus on the irritant and asthma-related effects of formaldehyde, for which they concluded "the evidence for differential effects is relatively weak,"[12] without mention of U.S. EPA's conclusion that more than 100 million people – including children – have a 10 in 1 million or higher cancer risk from formaldehyde exposure.[13] Indeed, OEHHA's decision to remove benzene and formaldehyde from Tier 1 is especially worrisome given the fact that of the 32 hazardous air pollutant addressed by the EPA in its Draft *National-Scale Air Toxics Assessment*, the Agency concluded that "those that appear to pose the greatest health threats to individuals (from inhalation exposure) in all parts of the U.S. are chromium, acrolein, *benzene*, *formaldehyde*, and carbon tetrachloride." (emphasis added).[14]

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[10] *See* National Academy of Sciences, *Multiple Chemical Sensitivities: Addendum to Biologic Markers in Immunotoxicology*, p. 23 (1992) (summarizing evidence that led the NAS in 1981 to conclude that formaldehyde causes bronchial asthma in humans).

[11] *Id.*

[12] *Prioritization* at 35; *But see*, National Academy of Sciences, *Clearing the Air: Asthma and Indoor Air Exposures*, p. 12 (2000) (noting that "non-specific respiratory tract irritants" can exacerbate asthma).

[13] EPA, *Draft National-Scale Air Toxics Assessment for 1996* at 95.

[14] *Id.* at 124.

Response Ic: There is evidence for differential effects of formaldehyde in children relative to adults, but it is relatively weak. OEHHA agree that the Krzyzanowski study indicates a greater response in children in terms of lung function decrement than adults in the same household. Interpretation of this result is somewhat complicated in that the effect is only seen in children who are also exposed to ETS at home. The comment quotes a National Academy of Sciences document as supporting a differential impact on children. This NAS quote is a recounting of the results of Krzyzanowski, and is not a separate study with the same conclusion.

The comment also implies that formaldehyde is associated with exacerbation of asthma. The data on exacerbation of asthma by formaldehyde indicate that only those asthmatics sensitized to formaldehyde from previous occupational exposures respond to formaldehyde with an asthma exacerbation. Thus, this exacerbation does not seem to be applicable to children. For this reason, formaldehyde was not placed in the first listing of up to 5 TACs under SB 25.

The comment also points out that the U.S. EPA's estimate of cancer risk from formaldehyde in ambient air is relatively high for many people. We agree that this is the case. However, the cancer risk from diesel exhaust particulate matter is even higher. Furthermore, the EPA's National Air Toxics Assessment quoted in the comment did not evaluate the cancer risks from exposure to diesel exhaust in ambient air.

Comment ID: Finally, OEHHA has acted inconsistently in how it has reviewed one of its statutorily mandated factors, the "extent of exposure and/or the magnitude of risk estimated to occur at concentrations typical of California urban ambient air."[15] Specifically, OEHHA has refused to consider the impact of extensive existing and planned controls on diesel particulate, claiming that it "was not directed to consider present or potential risk management programs during the prioritization process."[16] Despite OEHHA's claim, it is obvious that an analysis of exposure is incomplete without a consideration of existing real-world controls on the chemical – and an analysis of risk cannot occur without consideration of exposure levels. Moreover, in discussions with the SRP, OEHHA has factored the extent of control measures in its evaluation of other TACs. For instance, in its discussion of acrolein, at least one SRP Board member supported placing acrolein in Tier 1 because of "the potency of its irritancy, the scenarios for exposure…and its relative under-attention from a regulatory point of view."[17] If

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15 *Prioritization* at 10.

16 OEHHA's Responses to Comments Submitted by International Truck and Engine Corporation. ITEC – 8 (2001).

17 Transcript of the Meeting of the Scientific Review Panel on Toxic Air Contaminants at 202 (April 27, 2001).

OEHHA considers the level of regulatory attention to one TAC, it should consider the level of regulatory attention for all TACs.

Response ID: As noted in response Ia above, OEHHA specifically considered measurements of exposure in ambient air and estimates of emissions from stationary and mobile sources in evaluating TACs for listing under SB 25. The comment appears to imply that we did not consider existing exposures. We did indeed. The comment also seems to think we should consider "real-world controls on the chemical". While there is a large effort undertaken at the present by the Air Resources Board to evaluate management options for reducing emissions of diesel exhaust particulate matter, these controls are not yet in place and will be phased in over several years. Our job is not to evaluate effectiveness of risk management strategies but rather to determine whether we think exposure to a specific TAC will result in differential impacts on infants and children.

Comment II. The Science Does Not Support a Listing of Diesel Particulate in Tier 1.

Comment IIA: OEHHA cites to three reasons for listing diesel particulate in Tier 1: (1) "diesel exhaust particulate contains [polycyclic aromatic hydrocarbons] PAHs"; (2) "diesel exhaust particles contribute to ambient PM10" (particulate matter sized 10 microns or less), and (3) "diesel exhaust particulate can enhance allergic responses, and induce new allergies to airborne allergens."[18] In response to criticisms about OEHHA's reliance on PM and PAHs as its main rationales for listing diesel particulate in Tier 2 in its March Prioritization, OEHHA has since brought asthma-related illnesses to the forefront while simultaneously elevating diesel particulate to Tier 1. It is apparent from the record that asthma is now the primary reason for listing diesel particulate in Tier 1.

We have addressed OEHHA's PAH and PM arguments in previous comments[19]; the following discussion explains why the available data do not support a conclusion that diesel particulate induces or exacerbates asthma at ambient exposure levels, or that diesel particulate induces or exacerbates asthma differentially in children as compared to adults.

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[18] *Prioritization* at 35.

[19] Additionally, it is important to note that OEHHA is misplaced in its reliance on the Sato, et al. (2000) study to support the bioavailability of PAHs in its Responses to International Truck and Engine Corporation's Comments. In that mutagenicity study, scientists used whole diesel exhaust instead of diesel particulate, such that the study can say nothing about bioavailability of PAHs in diesel *particulate*. Furthermore, there was an absence of mutations at exposure levels far above ambient levels of diesel exhaust. Indeed, mutations were seen only at levels above the threshold of "lung overload," such that the observed mutations in lung DNA were likely the sequellae of lung overload, and not attributable to PAHs per se, either from the vapor or from the particulate phase. Numerous studies have shown that the influx of inflammatory cells into rat lungs produces mutations. *See*, *e.g.*, Driscoll, K.E., Deyo, L.C., Carter, J.M., Howard, B.W., Hassenbein, D.G., and Bertram, T.A. 1997. Effects of particle exposure and particle-elicited inflammatory cells on mutation in rat alveolar epithelial cells. Carcinogenesis 18:423-430.

The comments make four primary points: (1) the available data show allergic responses only at exposures far exceeding ambient levels; (2) OEHHA has failed to present studies that do not support its findings; (3) much of the data cited by OEHHA does not distinguish diesel particulate from other potential causative agents; and (4) absolutely no evidence exists to suggest that diesel particulate causes differential adverse effects in children.

Response IIA: Exacerbation of asthma and other allergen-related diseases is one of the reasons diesel exhaust particulate matter was listed in Tier 1 of the Prioritization. The other reasons include the higher dose rate of particles to children's lungs, the polycyclic aromatic hydrocarbon content of DEP, the observation of cancer in humans exposed to diesel exhaust, the evidence of lung function decrement in children from traffic studies, and studies of effects of PM_{10} on infant and child health including mortality. These reasons were not ranked in priority order, and all should be considered important in prioritizing diesel exhaust particulate matter under SB25.

Comment IIB: *The Available Data Show Allergic Responses Only At Exposures Far Exceeding Ambient Levels.* All the asthma and respiratory tract immune effects cited by OEHHA were observed in experiments with exposures far exceeding what anyone would see in Los Angeles, the city with the worst air quality in California. For instance, in one paper cited by OEHHA, Kobayashi et al. (1997) exposed guinea pigs via inhalation to exposure levels that ranged from 300 to 1000 times the estimated average exposure concentration in Los Angeles. Although the study found enhanced allergic responses to intra-nasally administered histamine at an exposure level 1000 times that in Los Angeles, it is significant that there was no effect at a level 300 times the exposures in Los Angeles. In fact, OEHHA also fails to cite studies with lower exposure levels that showed no effect.[20] As our June 12 comments have previously explained, OEHHA has also overstated these studies and their support for exacerbation of asthma.[21]

Response IIB: As noted in the response to International's prior comments, diesel exhaust particulate matter causes adverse immune system effects which may result in adverse health outcomes (e.g. possible exacerbation of asthma and allergic rhinitis) (Diaz-Sanchez *et al*., 2000; and many others, see summary for diesel); these adverse immunological effects are not shared by other model particulates such as carbon black and crystalline silica (van Zijverden *et al*., 2000). Acute exposures of healthy adult humans to concentrations of diesel exhaust particulate matter (300 $\mu g/m^3$) approximately

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[20] *See*, *e.g*., A.J. Frew, S. Salvi, S.T. Holgate, F. Kelly, N. Stenfors, C. Nordenhäll, A. Blomberg, T. Sandström. Low concentrations of diesel exhaust induce a neutrophilic response and upregulate IL-8 mRNA in healthy subjects but not in asthmatic volunteers. International Archives of Allergy and Immunology 124:1-3:2001, 324-325.

[21] International Truck and Engine Corporation's Comments to the SRP on Asthma Prevalence in Children and the Role of Diesel Exhaust in Asthma. p. 2 (June 12, 2001).

one order of magnitude greater than peak diesel exhaust concentrations noted near California freeways demonstrated a marked leukocytic airway infiltration accompanied by enhanced chemokine and cytokine production (Salvi *et al.*, 2000). It should be noted that 300 $\mu g/m^3$ was a LOEL (Lowest Observable Effect Level) in this study. Lower concentrations of diesel exhaust particulate matter were not tested, raising the possibility that these effects may be observed at concentrations lower than 300 $\mu g/m^3$. Additionally, the study by Frew *et al.* (2001) cited by the commenter as a negative study is in fact a positive study; they observed upregulation of IL-10 production in the bronchial epithelium of asthmatic subjects but not healthy subjects at a PM_{10} concentration of only 108 $\mu g/m^3$. The authors stated that the observed IL-10 upregulation may alter the airway biology towards a more allergic phenotype. It is also possible that healthy and/or asthmatic children may be more sensitive to diesel exhaust particulate matter-induced immune system effects than healthy adults. These data indicate that diesel exhaust particulate matter adversely impacts healthy adult immune systems at concentrations close to those observed in cars driving on California freeways (25 $\mu g/m^3$), making them very relevant to a consideration of diesel exhaust particulate matter for prioritization under SB 25. In addition, since there is a lag time for particle clearance, cumulative exposures occur routinely just by breathing the air in Los Angeles or other polluted metropolitan areas.

Comment IIC: *OEHHA Has Failed To Present Studies That Do Not Support Its Findings.* OEHHA has also selectively relied upon the database surrounding particulate matter, failing to present studies that contradict its findings.[22] Moreover, simple logic strongly suggests that diesel particulate is *not* responsible for the increasing incidence of asthma among children (and the general population). Specifically, the increased prevalence of asthma among children is occurring at the same time that the amount of diesel particulate matter in the ambient air – as well as PM levels – is decreasing

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[22] *See*, *e.g.*, G. Berit, P. Gaarder, E. Groeng, R. Leikvold, E. Namork, M. Løvik. Fine particles of widely different composition have an adjuvant effect on the production of allergen-specific antibodies. Toxicology Letters 115: 171-181, 2001. OEHHA also confuses whole diesel exhaust with diesel particulate. For example, it cites to diesel exhaust's contribution to other toxins such as benzene as additional support for its listing when, as their own report later states, benzene is a component of diesel *exhaust*, not diesel particulate, the TAC at issue. OEHHA's Responses to Comments from ITEC, ITEC-13. Later, OEHHA states that "while this study [Oosterlee] did not directly measure DEP, diesel exhaust is a major component of traffic-related pollution in the Netherlands, including NO_2, the pollutant modeled in this study." *Prioritization* at Appendix C-1, Diesel Exhaust Particulate Matter – 17. This in itself seems to support our argument of the numerous other pollutants at work in particulate matter, such as NO_2, that conflate any attempts to directly implicate diesel particulate.

substantially.[23] This inverse relationship argues against a causal relationship between diesel particulate (or particulate matter generally) and asthma incidence.[24]

A more scientific approach to assessing the asthma problem would be to look for factors – whether pollutants or otherwise – that have increased at the same time that asthma incidence has increased. For example, numerous studies have shown an association between obesity and development of asthma.[25] Obesity in children has been increasing at a high rate[26] – indeed, at a rate similar to the rate of increasing asthma incidence in children. Although it is currently not known whether the increasing incidence of obesity in the U.S. is responsible for increasing asthma rates, studies have suggested that this is the case,[27] and such an explanation makes more sense than claiming that rapidly decreasing levels of diesel particulate are causing increased rates of asthma.[28]

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23 EPA. Emissions Standards Reference Guide for Heavy-Duty and Nonroad Engines. (September 1997). In fact, emissions rates of diesel particulate have decreased 90% since 1980.

24 Casting further doubt on the link between asthma and diesel particulate is the fact that OEHHA estimates diesel particulate to contribute only "5% or so" of the total PM in California. *Prioritization* at Appendix C-1, Diesel Exhaust Particulate Matter - 19. As discussed in our April 6, 2001 comments, this weakens attempts to link diesel particulate to health-related effects from PM generally because of the existence of other air pollutants that contribute 95% of the California PM.

25 *See, e.g.,* Stenius-Aarniala B et.al. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. British Medical Journal 320: 827-832, 2000; P.F. Belamarich, E. Luder, M. Kattan, H. Mitchell, S. Islam, H. Lynn, et al. Do obese inner-city children with asthma have more symptoms than nonobese children with asthma? Pediatrics 106: 1436-41, 2000. *See also*, note 28.

26 The Weight-control Information Network (WIN), a national information service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH) states that prevalence of overweight in children has more than doubled between 1960 and 1994. NIDDK. Statistics Related to Overweight and Obesity, *available at* http://www.niddk.nih.gov/health/nutrit/pubs/statobes.htm#11 . *See also,* National Center for Health Statistics. 1999 National Health and Nutrition Examination Survey. Prevalence of Overweight Among Children and Adolescents: United States, 1999, *available at*: http://www.cdc.gov/nchs/products/pubs/pubd/hestats/overwght99.htm.

27 *See, e.g.*, C.A. Camargo, S.T. Weiss, S. Zhang, W.C. Willett, and F.E. Speizer. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. Archives of Internal Medicine 159(21): 2582-8, 1999; S.O. Shaheen, J.A. Sterne, S.M. Montogomery, and H. Azima. Birth weight, body mass index and asthma in young adults. Thorax 54(5): 396-402, 1999.

28 Similarly, both the U.S. EPA and the National Academy of Sciences have focused heavily on indoor exposures as the key to the increasing asthma incidence in the U.S. population. *See*, National Academy of Sciences, *Clearing the Air: Asthma and Indoor Air Exposures* (2000). As the NAS notes, "individuals spend nearly all of their time indoors . . . [and] many of the exposures thought to be associated with asthma occur predominantly indoors." *Id.* at 1. Indeed, the available data show that most people spend only 10% of their time (2.4 hours per day) or less outdoors. *See* National Academy of Sciences, *Multiple Chemical Sensitivities: Addendum to Biologic Markers in Immunotoxicology*, p. 20 (1992) (Table showing contribution of various

Response IIC: There are now several dozen studies which demonstrate that exposure to diesel exhaust particulate matter enhances the allergic response to allergens. In our search of the literature, we did not find any purely negative studies on allergenicity of diesel exhaust particles, although some studies found effects on one parameter indicating enhanced allergenicity but not necessarily on all parameters measured in the studies. The study cited by the comment in footnote 20 (Frew et al, 2001) is in fact not a negative study (see response IIb). The OEHHA document discusses the uncertainties associated with the adverse health effects reported for the TACs, and includes descriptions of negative studies where appropriate. However, it is not necessary to include a detailed description of every negative study for the prioritized TACs in the literature.

The commenter suggests that a statistical correlation exists between obesity and asthma in children and that exploring such a relationship makes better scientific sense than postulating that a relationship exists between diesel exhaust particulate matter exposure and asthma. Firstly, OEHHA has not stated that diesel exhaust exposure causes asthma or is responsible for the increasing asthma prevalence seen in the U.S. It is generally recognized that asthma causation is multifactorial. The comment cites studies correlating obesity with asthma. There are also studies correlating a number of environmental factors and poverty with asthma prevalence and exacerbation. In addition, assuming that there is a relationship between asthma and obesity, it seems more likely that asthma is a factor in causing obesity, since asthmatic children tend to be less active than healthy children, and lack of exercise has been well demonstrated to be a casual factor for obesity. It should be noted that OEHHA is concerned about exacerbation of existing asthma by diesel exhaust particulate matter and has emphasized that concern in the document. Causation of new cases is much more difficult to evaluate. However, since diesel exhaust particulate matter can enhance allergic responses even to neoallergens, exposure to DEP may contribute to the development of new asthma. OEHHA has also noted in the prioritization document and in its response to comments that no direct epidemiological evidence of differential sensitivity of children to asthma induced specifically by diesel exhaust particulate matter (as opposed to PM_{10} or $PM_{2.5}$) has been published. As stated in the introduction sections of our document, asthma is considered by OEHHA to be a disease that impacts children more than adults because:1) asthma prevalence rates are higher in children than adults; 2) hospitalization rates are highest for 0 to 4 year olds than other age groups; 3) children have smaller airways than adults and thus are more prone to serious breathing difficulty during an asthma attack (resistance is inversely proportional to the fourth power of the radius). The possibility that diesel exhaust particulate matter may exacerbate asthma (and thus differentially impact children) stems from the mechanistic data indicating that diesel exhaust particulate matter exerts specific adverse immune system effects (enhancing allergic responses in the

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atmospheric environments to average exposure). Because of their prevalence, indoor air exposures are more likely to be the causative agent in asthma induction or exacerbation than outdoor exposures.

airway; pages 7-13 in the diesel exhaust particulate matter summary), and the increasing number of studies linking PM_{10} exposure (of which diesel exhaust particulate matter is a component) with exacerbation of asthma (see pages 18 and 19 of the diesel exhaust particulate matter summary).

Comment IID: *Much Of The Data Cited By OEHHA Does Not Distinguish Diesel Particulate From Other Potential Causative Agents.* There are two areas where OEHHA has particularly speculative evidence for diesel particulate's impact on childhood asthma – the epidemiological studies relating to areas with high traffic ("traffic studies") and those that link PM generally with asthma. Neither data set has any ability to separate effects of diesel particulate from effects of the numerous other air pollutants involved. For instance, the traffic studies looked at effects near heavily trafficked areas – where diesel particulate is just one of many air pollutants present. The studies made no effort to identify which of the many air pollutants might have been responsible for the asthma-related effects, making these studies far weaker evidence for listing diesel particulate in Tier 1 than the evidence that OEHHA judged insufficient for listing benzene or formaldehyde in Tier 1.[29]

Similarly, OEHHA points to studies linking PM generally to asthma as support for diesel particulate's link to asthma.[30] Yet not one of these studies cited is able to distinguish between the numerous components of PM to know which of the constituents actually is the cause of the effects observed. The only evidence that OEHHA has for attributing any and all harmful effects of PM to diesel is that diesel is a constituent of PM. This ignores the commonly-known complications involved with particle size, distribution and other variables – all of which prevent being able to point to diesel particulate as the causal factor over a number of other PM constituents such as SO_2 or

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[29] Moreover, if OEHHA continues to rely on the traffic studies, it must also consider other traffic studies which present contrary findings. *See, e.g.,* M.H. Wieringa, P.A. Vermeire, H.P. Van Bever, V.J. Nelen, J.J. Weyler. Higher occurrence of asthma-related symptoms in an urban than a suburban area in an urban than a suburban area in adults, but not in children. European Respiratory Journal, 17: 422-427, 2001; T. Hirsch, S.K Weiland, E. Mutius, A.F. Safeca, H. Gräfe, E. Csaplovics, H. Duhme, U. Keil, W. Leupold. Inner city air pollution and respiratory health and atopy in children. European Respiratory Journal, 14: 669-677, 1999; G.P. Bonne, P.K. Mueller, L.W. Chen, B.G. Doddridge, W.A. Butler, P.A. Zawadzki, J.C. Chow, R.J. Troop, and S. Kohl. Composition of $PM_{2.5}$ in the Baltimore-Washington Corridor. Presented at *PM2000: Particulate Matter and Health*, Charleston, SC, January 24-28, 2000; and A.G. Miguel, G.R. Cass, M.M.. Glovsky, and J. Weiss. Allergens in Paved Road Dust and Airborne Particles. Environ Sci Technol 33(23): 4159-4168, 1999. This study enumerated the components in road dusts (as distinct from exhaust particles) present near Southern California roads, including pollen fragments, animal dander, and molds, all of which were made airborne by passing traffic. The authors concluded that "…paved road dust when entrained into the atmosphere by passing traffic is a source of allergen exposure for the general population…"

[30] As discussed in our June 12 comments, even the research literature on the role of PM in asthma exacerbation has many gaps.

NO_x.[31] And again, OEHHA's evidence is far weaker than the evidence associated with benzene and formaldehyde.[32]

Response IId: The comment points out the difficulty of evaluating epidemiological studies to pinpoint causative agents. However, the statute requires OEHHA to consider multiple pollutant exposures. Therefore, if there is an association between PM_{10} and other co-pollutant and an adverse health effect, that information must still be considered. Most of the studies that looked at respiratory health impacts of traffic-related pollutants specifically looked at truck traffic, which in the countries where the studies were done is predominantly diesel-fueled. Truck traffic density was the metric associated with adverse respiratory health impacts. In addition, one of the studies measured PM_{10} and soot (largely $PM_{2.5}$) as well as truck traffic density. The strongest correlation with adverse respiratory health impacts in this study (Brunekreef et al, 1996) was with soot. Thus, the comment overstates the problem of being unable to distinguish between the effects of co-pollutant exposure (confounding or effect modification) and underestimates the ability of these traffic studies to provide evidence for particulate pollution as a causative factor in the adverse respiratory health impacts observed in children in these studies.

The comment also overstates the problem of co-pollutant confounding in the PM_{10} and asthma studies. The comment states that "not one of these studies cited is able to distinguish between the numerous components of PM to know which of the constituents actually is the cause of the effects observed", and notes that this "prevents being able to point to diesel particulate as the causal factor over a number of other PM constituents such as SO_2 or NOx". There are now a dozen or more studies which evaluated exacerbation of symptoms in asthmatics and air pollution. Many of these studies find a positive association with PM_{10}. These studies were done in Europe, the U.S., Mexico, and British Columbia in areas with very different mixes of pollutants. However, the varied environments studied provide support that the PM_{10} associations are quite real. The California studies were done in locations that have ozone and NO_2 but very little SO_2 present in the pollutant mix; the British Columbia sites have little ozone, SO_2 or NO_2 in the pollutant mix; East Coast studies have lower NO_2 and higher SO_2 than West Coast cities. While a number of pollutants have been shown to exacerbate asthma in both chamber studies and in epidemiological investigations (SO_2, NO_2, ozone), the fact that positive associations between asthma symptoms and particulate matter are found in studies with very different co-pollutant mixes argues strongly that the exacerbation of symptoms in asthmatics observed in these studies is at least in part due to exposure to PM_{10}. As already noted, SB 25 requires consideration of effects from multiple exposures

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[31] The NAS has identified an association ("sufficient evidence of an association") between high levels of NO_x in indoor air and exacerbation of asthma. National Academy of Sciences, *Clearing the Air: Asthma and Indoor Air Exposures*, p. 9 (2000).

[32] Indeed, as discussed above, the NAS has concluded that formaldehyde can cause bronchial asthma in humans. *See supra*, note 11.

including exposures to Criteria Air Pollutants. Thus, if the effects on asthmatics from air pollutants including PM_{10} involve interactions, a strong possibility, then this needs to be considered in listing chemicals under SB 25, and is definitely not a reason to exclude listing a TAC under SB 25. In addition, in some of these cities, the ambient PM_{10} was largely diesel exhaust particulate. Thus, it is difficult to discount the effects as being attributable to something else and that diesel exhaust particulate has no role whatsoever.

Comment IIE: *Absolutely No Evidence Exists To Suggest That Diesel Particulate Causes Differential Adverse Effects In Children.* Even if diesel particulate is capable of inducing or exacerbating asthma, there is no evidence that diesel particulate has a differential impact on children. Unlike both formaldehyde and benzene, for which there are studies showing differential adverse impacts in children, for diesel particulate, OEHHA relies only on the following speculation: (1) the prevalence of asthma is much higher among children than among adults; (2) the smaller airways of children predispose them to more severe attacks; and (3) children in age group 0 to 4 are hospitalized for asthma more frequently than any other age group.[33] Yet these findings together cannot support a conclusion that diesel particulate has a differential effect on children over adults – and they certainly constitute far weaker evidence of differential effects than is available for benzene and formaldehyde.

As discussed above, the increased prevalence of asthma in children is certainly a concern, but it is difficult to identify a logical justification for attributing this increase to diesel particulate when exposures to diesel particulate have been decreasing dramatically at the same time that prevalence of asthma in children has been increasing. With regard to children's smaller airways and increased breathing rates,[34] the American Council on Science and Health has concluded that:

> Aside from assumptions about a child's developing body, narrower airways, faster metabolism, and increased breathing rates, no studies are known to exist that support the contention of greater child susceptibility. In fact, the opposite argument could be made - that differential physiological characteristics in children...result in reduced

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[33] *Prioritization* at 27-28. The only study cited that provides an actual comparison between children and adults is the Oosterlee, et al. (1996) traffic study. However, OEHHA has admitted that this traffic study is not able to narrow the respiratory impacts of traffic related pollutants down to diesel exhaust specifically and therefore "can't call it conclusive evidence." Transcript of the Meeting of the Scientific Review Panel on Toxic Air Contaminants at 165 (May 14, 2001). OEHHA even states that "the precise role (if any) of diesel exposure in the development of atopy has not been defined…" *Prioritization* at Appendix C-1, Diesel Exhaust Particulate Matter – 28.

[34] OEHHA has no studies to support this hypothesis, yet cites to their previous review of the prioritization of Criteria Air Pollutants under SB 25 by the Air Quality Advisory Committee. *Prioritization* at Appendix C-1, Diesel Exhaust Particulate Matter – 20-21.

> penetration of DE particulates to the deep lung, and that faster metabolism or lymphatic clearance may result in increased clearance of particulate matter.[35]

Lastly, the hospitalization data is a far cry from concrete evidence that diesel particulate may cause children to be more susceptible to illness, especially given behavioral complications surrounding such a finding (many parents have greater concern for their smaller children, not necessarily implying the greatest risk group, but merely those that are brought to a hospital for treatment).

Perhaps as a result of the paucity of evidence of differential effects, in the case of diesel particulate, at least, OEHHA has strayed from its statutory mandate. The Children's Environmental Health Protection Act ("SB 25") requires OEHHA to list up to five TACs that "may cause infants and children to be especially susceptible to illness." In the case of diesel particulate, OEHHA has chosen a specific pathology – asthma – that it claims appears differently in children than in adults. OEHHA does not have scientific data linking diesel particulate to increased susceptibility in children but instead has identified what it claims to be a childhood pathology – an action which is outside the scope of its statutory authority. This strategy is similarly unconvincing as support for inclusion of diesel particulate in Tier 1.[36]

Response IIE: The comment seems to indicate OEHHA believes that the increased prevalence rates of asthma in children relative to adults is due to diesel exhaust exposure. We have made no such statement nor drawn such a conclusion. The prevalence rate data themselves simply show a higher prevalence of asthma in children relative to adults. Thus children as a population are impacted by asthma, and therefore by TACs that exacerbate asthma, to a greater extent than adults. The argument OEHHA is making that children's smaller airways contribute to a worse outcome for asthma attacks than adults is not predicated upon an exposure difference as indicated in the comments. Rather the smaller airway argument is based on simple physics. The resistance to airflow is inversely proportional to the fourth power of the radius. A larger airway provides less resistance to airflow. If a larger airway constricts, the effect is less dramatic than if a smaller airway constricts. Breathing difficulty during an asthma attack can be a bigger problem in young asthmatics than in adult asthmatics. Finally, the comment implies that children are hospitalized at higher rates due to asthma attacks because parents are more

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[35] Daland R. Juberg. *School Buses and Diesel Fuel.* American Council on Science and Health. (June 2001), *available at* http://www.acsh.org/publications/reports/school_buses.html.

[36] Moreover, even if it were appropriate for OEHHA to target a childhood pathology rather than TACs that differentially affect children, it certainly would be arbitrary for OEHHA to include diesel particulate on Tier 1 because of its alleged contribution to that pathology, while ignoring formaldehyde – which the NAS has identified as causing asthma, which is ubiquitous in the indoor environments in which people spend most of their time, and which has been shown to specifically impact children.

concerned about kids and therefore bring them to the hospital. While a number of factors influence who seeks treatment for asthma, hospitalization data reflect a physician's decision to hospitalize, not a parent's decision to seek treatment. Hospitalization is, therefore, not a discretionary event, and only occurs in severe cases. Rather, the fact that 0 to 4 year olds are hospitalized at a greater rate than any other age group corresponds to the physics of resistance to airflow being inversely proportional to the fourth power of the radius.

Comment III: OEHHA's Procedural Defects Have Undermined the Credibility of the SB 25 TAC Listing Process.

OEHHA's decisions surrounding the final comment period and its deference to the wishes of SRP cast doubt on the procedural integrity of this Tier 1 prioritization process. The Prioritization invokes the procedural safeguards of the California Administrative Procedure Act ("APA"),[37] which, at a minimum, requires OEHHA to give notice and provide a period for public comment on the revised Prioritization *prior* to its adoption. Yet, in an effort to meet the July 1, 2001 statutory deadline, OEHHA chose to issue the revised Prioritization without providing such an opportunity for public review. Instead, OEHHA adopted the Prioritization subject to a comment period that is scheduled to close on July 13, 2001 – 12 days *after* OEHHA was required by SB 25 to issue the Prioritization. By scheduling a post hoc period of "reconsideration," rather than a meaningful period for public comment, OEHHA violated the APA.

Moreover, despite SB 25's express requirement that OEHHA "establish"[38] the Prioritization of TACs, the SRP revised the Prioritization at its June 15, 2001 meeting, and OEHHA merely "rubber-stamped" the revision without engaging in a critical review of the changes made to the TAC listing.[39] OEHHA acquiesced in the SRP's revisions to the TAC listing, without further scientific review and absent any oversight by Joan Denton, Director of OEHHA, who was not present at the meeting. By revising the TAC listing, the SRP exceeded its statutory authority to merely "review"[40] the Prioritization, not to modify the TAC listing on its own accord. At the same time, OEHHA improperly failed to "establish" the Prioritization, contrary to the language of SB 25.

Response III: The comment indicates a misunderstanding of the process of peer review under SB 25 conducted by the SRP, and the activities and results of the June 15, 2001 SRP meeting. Health and Safety Code Section 39669.5 requires OEHHA to establish a

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37 The Prioritization invokes these procedural safeguards because it reflects an exercise of quasi-legislative power by OEHHA and qualifies as a regulation under the APA.

38 CAL. HEALTH & SAFETY CODE § 39669.5(a)(1).

39 Although OEHHA entered this meeting with diesel particulate in Tier 2, the SRP members proposed to elevate diesel particulate to Tier 1 and drop benzene and formaldehyde to Tier 2 before OEHHA was even able to discuss its current assessment of diesel particulate.

40 CAL. HEALTH & SAFETY CODE § 39669.5(a)(2).

list of up to five TACs that may cause infants and children to be especially susceptible to illness. OEHHA must provide the list and a report containing its reasons for including the TACs on the list to the Scientific Review Panel. The SRP "in a manner consistent with this chapter[3.5], shall review the list of toxic air contaminants submitted by the office [OEHHA]…" Thus, the SRP must provide comment and develop findings as they do for any Toxic Air Contaminant identification document. There were three meetings of the SRP devoted to discussion of the issues in the OEHHA document and development of the list by OEHHA. OEHHA revised the document per the discussions at the SRP meetings and also per public comment. The SRP did not revise the list. The SRP voted to provisionally approve OEHHA's proposed revised list at the June 15th SRP meeting pending another public comment period. Thus, the comment's contention that OEHHA adopted the prioritization prior to public comment is incorrect. OEHHA has not yet adopted the list of up to five TACs. The Director of OEHHA is awaiting the results of the final public comment period and evaluating the information from the most recent SRP meeting before establishing a list.

The comment also appears to imply that the development of the list by OEHHA of five TACs that may cause infants and children to be especially susceptible to illness is subject to the Administrative Procedure Act ("APA"). However, the APA does not apply to the SB 25 listing activity undertaken by OEHHA. That is, the list of five TACs developed by OEHHA is not the adoption of "regulation[s]" as that term is defined by Government Code Section 11342(g). The list created by OEHHA does not subject any entities to any duties. Nor does it in any way limit the activities of any entities. Rather, consistent with the general TAC program, the rulemaking activity will be undertaken by the ARB at such time as it adopts any regulations setting standards regarding this subset of TACs. State agencies are not required to engage in serial rulemaking for a component of a more comprehensive rulemaking effort. This is especially true when, as in this case, the initial component is not itself a "regulation" within the meaning of the APA.